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(54) Title: A MODIFIED POLYPEPTIDE WITH REDUCED IMMUNE RESPONSE

(57) Abstract

The present invention relates to polypeptides with reduced immune response including reduced allergenicity having one or more amino acid residues being substituted with other amino acid residues and/or having coupled one or more polymeric molecules in the vicinity of the polypeptides metal binding site, a method for preparing modified polypeptides of the invention, the use of said polypeptide for reducing the immunogenicity and allergenicity and compositions comprising said polypeptide.

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Title: A MODIFIED POLYPEPTIDE WITH REDUCED IMMUNE RESPONSE

FIELD OF THE INVENTION

The present invention relates to polypeptides having substituted one or more amino acid residues to said polypeptide and/or having coupled polymeric molecules on the surface of the 3-dimensional structure of the polypeptide, a method for preparing modified polypeptides of the invention, the use of said modified polypeptides for reducing the immunogenicity and allergenicity, and compositions comprising said polypeptide.

BACKGROUND OF THE INVENTION

The use of polypeptides, including enzymes, in the circulatory system to obtain a particular physiological effect is well-known in the medical arts. Further, within the arts of industrial applications, such as laundry washing, textile bleaching, personal care, contact lens cleaning, and food and feed preparation enzymes are used as a functional ingredient. One of the important differences between pharmaceutical and industrial application is that for the latter type of applications (*i.e.* industrial applications) the polypeptides (often enzymes) are not intended to enter into the circulatory system of the body.

Certain polypeptides and enzymes have an unsatisfactory stability and may under certain circumstances - dependent on the way of challenge - cause an immune response, typically an IgG and/or IgE response.

It is today generally recognized that the stability of polypeptides is improved and the immune response is reduced when polypeptides, such as enzymes, are coupled to polymeric molecules. It is believed that the reduced immune response is a result of the shielding of (the) epitope(s) on the surface of the polypeptide responsible for the immune response leading to antibody formation by the coupled polymeric molecules.

Techniques for conjugating polymeric molecules to polypeptides are well-known in the art.

One of the first suitable commercially techniques was described back in the early 1970'ies and disclosed in *e.g.* US patent no. 4,179,337. Said patent concerns non-immunogenic polypeptides, such as enzymes and peptide hormones coupled to polyethylene glycol (PEG) or polypropylene glycol (PPG). At least 15% of the polypeptides' physiological activity is maintained.

GB patent no. 1,183,257 (Crook et al.) describes chemistry for conjugation of enzymes to polysaccharides via a triazine ring.

Further, techniques for maintaining of the enzymatic activity of enzyme-polymer conjugates are also known in the art.

WO 93/15189 (Veronese et al.) concerns a method for maintaining the activity in polyethylene glycol-modified proteolytic enzymes by linking the proteolytic enzyme to a macromolecularized inhibitor. The conjugates are intended for medical applications.

It has been found that the attachment of polymeric molecules to a polypeptide often has the effect of reducing the activity of the polypeptide by interfering with the interaction between the polypeptide and its substrate. EP 183 503 (Beecham Group PLC) discloses a development of the above concept by providing conjugates comprising pharmaceutically useful proteins linked to at least one water-soluble polymer by means of a reversible linking group.

EP 471,125 (Kanebo) discloses skin care products comprising a parent protease (*Bacillus* protease with the trade name Esperase®) coupled to polysaccharides through a triazine ring to improve the thermal and preservation stability. The coupling technique used is also described in the above mentioned GB patent no. 1,183,257 (Crook et al.).

JP 3083908 describes a skin cosmetic material which contains a transglutaminase from guinea pig liver modified with one or more water-soluble substance such as PEG, starch, cellulose etc. The modification is performed by activating the polymeric molecules and coupling them to the enzyme. The composition is stated to be mild to the skin.

WO 98/35026 (Novo Nordisk A/S) describes polypeptide-

polymer conjugates having added and/or removed one or more attachment groups for coupling polymeric molecules on the surface of the polypeptide structure. The conjugates have reduced immunogenicity and allergenicity.

SUMMARY OF THE INVENTION

It is the object of the present invention to provide improved polypeptides suitable for industrial and pharmaceutical applications.

The term "improved polypeptides" means in the context of the present invention polypeptides having a reduced immune response in humans and animals. As will be described further below the immune response is dependent on the way of challenge.

The present inventors have found that polypeptides, such as enzymes, may be made less immunogenic and/or allergenic by substituting one or more amino acid residues on the surface of the polypeptide with other amino acid residues and/or by coupling polymeric molecules on the surface of the enzyme in the vicinity of a bound ligand of the enzyme e.g. a metal ion substantially without affecting the enzymatic activity.

When introducing pharmaceutical polypeptide directly into the circulatory system (*i.e.* bloodstream) the potential risk is an immunogenic response in the form of mainly IgG, IgA and/or IgM antibodies. In contrast hereto, industrial polypeptides, such as enzymes used as a functional ingredient in *e.g.* detergents, are not intended to enter the circulatory system. The potential risk in connection with industrial polypeptides is inhalation causing an allergenic response in the form of mainly IgE antibody formation.

Therefore, in connection with industrial polypeptides the potential risk is respiratory allergenicity caused by inhalation, intratracheal and intranasal presentation of polypeptides.

The main potential risk of pharmaceutical polypeptides is immunogenicity caused by intradermal, intravenous or subcutaneous presentation of the polypeptide.

The term "immunogenicity" used in connection with the present invention may be referred to as allergic contact

dermatitis in a clinical setting and is a cell mediated delayed immune response to chemicals that contact and penetrate the skin. This cell mediated reaction is also termed delayed contact hypersensitivity (type IV reaction according to Gell and Combs classification of immune mechanisms in tissue damage).

The term "allergenicity" or "respiratory allergenicity" is initially an immediate anaphylactic reaction (type I antibody-mediated reaction according to Gell and Combs) following inhalation of *e.g.* polypeptides.

According to the present invention it is possible to provide polypeptides with a reduced immune response, which has a substantially retained residual activity.

The allergic and the immunogenic response are in one term, at least in the context of the present invention called the "immune response".

In the first aspect the invention relates to a polypeptide with reduced immune response, having one or more amino acid residues modified, wherein the C^{α}-atoms of said amino acid residues are located less than 15 Å from the ligand bound to said polypeptide.

The reduced immune response is preferably reduced allergenicity.

The modification of the polypeptide is conducted by substituting one or more amino acid residues in the parent polypeptide with other amino acid residues to said polypeptide, and/or by selecting variants from a diverse library of variants of the parent polypeptide and/or by coupling a polymeric molecule to the surface of the parent polypeptide.

The term "parent polypeptide" refers to the polypeptide to be modified by coupling to polymeric molecules or by substituting amino acid residues. The parent polypeptide may be a naturally-occurring (or wild-type) polypeptide or may be a variant thereof prepared by any suitable means. For instance, the parent polypeptide may be a variant of a naturally-occurring polypeptide which has been modified by substitution, deletion or truncation of one or more amino acid residues or by addition or insertion of one or more amino acid residues to the amino acid sequence of a naturally-occurring polypeptide.

A "suitable attachment group" means in the context of the present invention any amino acid residue group on the surface of the polypeptide capable of coupling to the polymeric molecule in question.

Preferred attachment groups are amino groups of Lysine residues and the N-terminal amino group. Polymeric molecules may also be coupled to the carboxylic acid groups (-COOH) of amino acid residues in the polypeptide chain located on the surface. Carboxylic acid attachment groups may be the carboxylic acid group of Aspartate or Glutamate and the C-terminal COOH-group. Another attachment group is SH-groups in Cysteine.

An "active site" means any amino acid residues and/or molecules which are known to be essential for the performance of the polypeptide, such as catalytic activity, *e.g.* the catalytic triad residues, Histidine, Aspartate and Serine in Serine proteases, or *e.g.* the heme group and the distal and proximal Histidines in a peroxidase such as the *Arthromyces ramosus* peroxidase.

A "ligand", means in the context of the present invention a metal or metal ion or a cofactor.

In the context of the present invention "modification of amino acid residues" means that amino acid residues are substituted with other amino acid residues and/or a polymeric molecule is coupled to the amino acid residue. The polypeptide of the present invention may according to the invention be modified by substitution alone, by coupling of a polymeric molecule alone or by a combination of substitution and coupling.

In the context of the present invention "located" means the shortest distance from any atom in the ligand to the relevant C-atom in the amino acid residue.

Furthermore, in the context of the present invention e.g. "R250K" means that the amino acid Arginine in position 250 of the polypeptide has been substituted with the amino acid Lysine according to the one-letter-code of amino acids.

In the second aspect the invention relates to a method for preparing polypeptides with reduced immune response comprising the steps of:

a) identifying amino acid residues located on the surface of the

3-dimensional structure of the parent polypeptide in question,

b) selecting target amino acid residues on the surface of said 3-dimensional structure of said parent polypeptide to be modified,

c) substituting one or more amino acid residues selected in step b) with other amino acid residue, and/or

d) coupling polymeric molecules to the amino acid residues in step b) and/or step c).

The invention also relates to the use of a modified polypeptide of the invention and the method of the invention for reducing the immunogenicity of pharmaceuticals and reducing the allergenicity of industrial products.

Finally the invention relates to compositions comprising a modified polypeptide of the invention and further ingredients used in industrial products or pharmaceuticals.

BRIEF DESCRIPTION OG THE DRAWINGS

Figure 1 shows integrated IgE antibudy levels in rats.

Figure 2 shows integrated specific IgE levels in mice.

DETAILED DESCRIPTION OF THE INVENTION

It is the object of the present invention to provide improved polypeptides suitable for industrial and pharmaceutical applications.

Even though polypeptides used for pharmaceutical applications and industrial application can be quite different the principle of the present invention may be tailored to the specific type of parent polypeptide (*i.e.* enzyme, hormone peptides etc.).

The present inventors have found that polypeptides, such as enzymes, may be made less immunogenic and/or less allergenic by substituting amino acid residues in the vicinity of the ligand e.g. metal ion at the metal ion binding site and/or by coupling one or more polymeric molecules on the surface of the parent polypeptide. In addition thereto the inventors have found that a high percentage of maintained residual catalytic activity may be maintained in these modified polypeptides.

In the first aspect the invention relates to an improved polypeptide having one or more amino acid residues modified,

wherein the C^{α}-atom of said amino acid residues is located less than 15 Å from the ligand bound to said polypeptide.

The substitution of amino acid residues and coupling of polymeric molecule may be carried out in a conventional manner as described below.

Reduced immune response vs. maintained residual enzymatic activity

For enzymes, there is a conflict between reducing the immune response and maintaining a substantial residual enzymatic activity.

Without being limited to any theory it is believed that the loss of enzymatic activity of enzyme-polymer conjugates might be a consequence of impeded access of the substrate to the active site in the form of spatial hindrance of the substrate by especially bulky and/or heavy polymeric molecules to the catalytic cleft. It might also, at least partly, be caused by disadvantageous minor structural changes of the 3-dimensional structure of the enzyme due to the stress made by the coupling of the polymeric molecules.

Also, polypeptides modified by substituting one or more amino acid residues may have reduced enzymatic activity.

Maintained residual activity

A modified polypeptide of the invention has a substantially maintained catalytic activity.

A "substantially" maintained catalytic activity is in the context of the present invention defined as an activity which is above 20%, at least between 20% and 30%, preferably between 30% and 40%, more preferably between 40% and 60%, better from 60% up to 80%, even better from 80% up to about 100%, in comparison to the activity of the modified polypeptide prepared on the basis of corresponding parent polypeptides.

In the case of polypeptide-polymer conjugates of the invention where no polymeric molecules are coupled at or close to the active site(s) the residual activity may even be up to 100% or very close thereto. If attachment group(s) of the parent polypeptide is(are) removed from the active site the activity

might even be more than 100% in comparison to modified (*i.e.* polymer coupled) parent polypeptide conjugate.

The attachment group

Virtually all ionized groups, such as the amino groups of Lysine residues, are located on the surface of the polypeptide molecule (see for instance Thomas E. Creighton, (1993), "Proteins", W.H. Freeman and Company, New York).

Therefore, the number of readily accessible attachment groups (*e.g.* amino groups) on a modified or parent polypeptide equals generally the number of Lysine residues in the primary structure of the polypeptide plus the N-terminus amino group.

The chemistry of coupling polymeric molecules to amino groups is quite simple and well established in the art. Therefore, it is preferred to add Lysine residues (*i.e.* attachment groups) to the parent polypeptide in question to obtain improved conjugates with reduced immunogenicity and/or allergenicity and/or improved stability and/or high percentage maintained catalytic activity.

Polymeric molecules may also be coupled to the carboxylic groups (-COOH) of amino acid residues on the surface of the polypeptide. Therefore, if using carboxylic groups (including the C-terminal group) as attachment groups addition and/or removal of Aspartate and Glutamate residues may also be a suitable according to the invention.

If using other attachment groups, such as -SH groups, they may be added and/or removed analogously.

Substitution of the amino acid residues is preferred over insertion, as the impact on the 3-dimensional structure of the polypeptide normally will be less pronounced.

The parent polypeptide

In the context of the present invention, the term "polypeptides" includes proteins, peptides and/or enzymes for pharmaceutical or industrial applications. Typically the polypeptides in question have a molecular weight in the range between about 1 to 1000 kDa, preferred 4 to 100 kDa, more

preferred 12 to 60 kDa.

Pharmaceutical polypeptides

The term "pharmaceutical polypeptides" is defined as polypeptides, including peptides, such as peptide hormones, proteins and/or enzymes, being physiologically active when introduced into the circulatory system of the body of humans and/or animals.

Pharmaceutical polypeptides are potentially immunogenic as they are introduced into the circulatory system.

Examples of "pharmaceutical polypeptides" contemplated according to the invention include insulin, ACTH, glucagon, somatostatin, somatotropin, thymosin, parathyroid hormone, pigmentary hormones, somatomedin, erythropoietin, luteinizing hormone, chorionic gonadotropin, hypothalmic releasing factors, antidiuretic hormones, thyroid stimulating hormone, relaxin, interferon, thrombopoietin (TPO) and prolactin.

Industrial polypeptides

Polypeptides used for industrial applications often have an enzymatic activity. Industrial polypeptides (*e.g.* enzymes) are (in contrast to pharmaceutical polypeptides) not intended to be introduced into the circulatory system of the body.

It is not very like that industrial polypeptides, such as enzymes used as ingredients in industrial compositions and/or products, such as detergents and personal care products, including cosmetics, come into direct contact with the circulatory system of the body of humans or animals, as such enzymes (or products comprising such enzymes) are not injected (or the like) into the bloodstream.

Therefore, in the case of the industrial polypeptide the potential risk is respiratory allergy (*i.e.* IgE response) as a consequence of inhalation of polypeptides through the respiratory passage.

In the context of the present invention "industrial polypeptides" are defined as polypeptides, including peptides, proteins and/or enzymes, which are not intended to be administered to humans and/or animals.

Examples of such polypeptides are polypeptides, especially enzymes, used in products such as detergents, household article products, agrochemicals, personal care products, such as skin care products, including cosmetics and toiletries, oral and dermal pharmaceuticals, composition use for processing textiles, compositions for hard surface cleaning, and compositions used for manufacturing food and feed etc.

Enzymatic activity

Pharmaceutical or industrial polypeptides exhibiting enzymatic activity will often belong to one of the following groups of enzymes including Oxidoreductases (E.C. 1, "Enzyme Nomenclature, (1992), Academic Press, Inc.), such as laccase and Superoxide dismutase (SOD); Transferases, (E.C. 2), such as transglutaminases (TGases); Hydrolases (E.C. 3), including proteases, especially subtilisins, and lipolytic enzymes; Isomerases (E.C. 5), such as Protein disulfide Isomerases (PDI).

Hydrolases

Proteolytic enzymes

Contemplated proteolytic enzymes include proteases selected from the group of Aspartic proteases, such as pepsins, Cysteine proteases, such as Papain, Serine proteases, such as subtilisins, or metallo proteases, such as Neutrase®.

Specific examples of parent proteases include PD498 (WO 93/24623 and SEQ ID NO. 2), Savinase® (von der Osten et al., (1993), Journal of Biotechnology, 28, p. 55+, SEQ ID NO 3), Proteinase K (Gunkel et al., (1989), Eur. J. Biochem, 179, p. 185-194), Proteinase R (Samal et al, (1990), Mol. Microbiol, 4, p. 1789-1792), Proteinase T (Samal et al., (1989), Gene, 85, p. 329-333), Subtilisin DY (Betzel et al. (1993), Arch. Biophys, 302, no. 2, p. 499-502), Lion Y (JP 04197182-A), Rennilase® (Available from Novo Nordisk A/S), JA16 (WO 92/17576), Alcalase® (a natural subtilisin Carlberg variant) (von der Osten et al., (1993), Journal of Biotechnology, 28, p. 55+), Subtilisin BPN´ J. Mol. Biol. 178:389-413 (1984); Hirono S., Akagawa H., Mitsui Y., Iitaka Y. (Available from Novo Nordisk A/S).

Carbohydrases

Parent carbohydrases may be defined as all enzymes capable of hydrolyzing carbohydrate chains (*e.g.* starches) of especially five and six member ring structures (*i.e.* enzymes classified under the Enzyme Classification number E.C. 3.2 (glycosidases) in accordance with the Recommendations (1992) of the International Union of Biochemistry and Molecular Biology (IUBMB)). Examples include carbohydrases selected from those classified under the Enzyme Classification (E.C.) numbers:

a-amylase (3.2.1.1) b-amylase (3.2.1.2), glucan 1,4-a-glucosidase (3.2.1.3), cellulase (3.2.1.4), endo-1,3(4)-b-glucanase (3.2.1.6), endo-1,4-b-xylanase (3.2.1.8), dextranase (3.2.1.11), chitinase (3.2.1.14), polygalacturonase (3.2.1.15), lysozyme (3.2.1.17), b-glucosidase (3.2.1.21), a-galactosidase (3.2.1.22), b-galactosidase (3.2.1.23), amylo-1,6-glucosidase (3.2.1.33), xylan 1,4-b-xylosidase (3.2.1.37), glucan endo-1,3-b-D-glucosidase (3.2.1.39), a-dextrin endo-1,6-glucosidase (3.2.1.41), sucrose a-glucosidase (3.2.1.48), glucan endo-1,3-a-glucosidase (3.2.1.59), glucan 1,4-b-glucosidase (3.2.1.74), glucan endo-1,6-b-glucosidase (3.2.1.75), arabinan endo-1,5-a-arabinosidase (3.2.1.99), lactase (3.2.1.108), chitonanase (3.2.1.132).

Examples of relevant carbohydrases include a-1,3-glucanases derived from *Trichoderma harzianum*; a-1,6-glucanases derived from a strain of *Paecilomyces*; b-glucanases derived from *Bacillus subtilis*; b-glucanases derived from *Humicola insolens*; b-glucanases derived from *Aspergillus niger*; b-glucanases derived from a strain of *Trichoderma*; b-glucanases derived from a strain of *Oerskovia xanthineolytica*; exo-1,4-a-D-glucosidases (glucoamylases) derived from *Aspergillus niger*; a-amylases derived from *Bacillus subtilis*; a-amylases derived from *Bacillus amyloliquefaciens*; a-amylases derived from *Bacillus stearothermophilus*; a-amylases derived from *Aspergillus oryzae*; a-amylases derived from non-pathogenic microorganisms; a-galactosidases derived from *Aspergillus niger*; Pentosanases,

xylanases, cellobiases, cellulases, hemi-cellulases deriver from *Humicola insolens*; cellulases derived from *Trichoderma reesei*; cellulases derived from non-pathogenic mold; pectinases, cellulases, arabinases, hemi-celluloses derived from *Aspergillus niger*; dextranases derived from *Penicillium lilacinum*; endo-glucanase derived from non-pathogenic mold; pullulanases derived from *Bacillus acidopullyticus*; b-galactosidases derived from *Kluyveromyces fragilis*; xylanases derived from *Trichoderma reesei*;

Specific examples of readily available commercial carbohydrases include Alpha-GalÔ, Bio-FeedÔ Alpha, Bio-FeedÔ Beta, Bio-FeedÔ Plus, Bio-FeedÔ Plus, Novozyme® 188, Carezyme®, Celluclast®, Cellusoft®, Ceremyl®, CitrozymÔ, DenimaxÔ, DezymeÔ, DextrozymeÔ, Finizym®, FungamylÔ, GamanaseÔ, Glucanex®, Lactozym®, MaltogenaseÔ, PentopanÔ, PectinexÔ, Promozyme®, PulpzymeÔ, NovamylÔ, Termamyl®, AMG (Amyloglucosidase Novo), Maltogenase®, Aquazym®, Natalase® (all enzymes available from Novo Nordisk A/S). Other carbohydrases are available from other companies.

It is to be understood that also carbohydrase variants are contemplated as the parent enzyme.

The activity of carbohydrases can be determined as described in "Methods of Enzymatic Analysis", third edition, 1984, Verlag Chemie, Weinheim, vol. 4.

Oxidoreductases

Laccases

Contemplated laccases include *Polyporus pinisitus* laccase (WO 96/00290), Myceliophthora laccase (WO 95/33836), Schytalidium laccase (WO 95/338337), and *Pyricularia oryzae laccase* (Available from Sigma).

Peroxidase

Contemplated peroxidases include *B. pumilus* peroxidases (WO 91/05858), *Myxococcaceae* peroxidase (WO 95/11964), *Coprinus*

cinereus (WO 95/10602) and *Arthromyces ramosus* peroxidase (Kunishima et al. (1994), J. Mol. Biol. 235, p. 331-344).

Transferases

Transglutaminases

Suitable transferases include any transglutaminases disclosed in WO 96/06931 (Novo Nordisk A/S) and WO 96/22366 (Novo Nordisk A/S).

Isomerases

Protein Disulfide Isomerase

Without being limited thereto suitable protein disulfide isomerases include PDIs described in WO 95/01425 (Novo Nordisk A/S).

Contemplated isomerases include xylose/glucose Isomerase (5.3.1.5) including Sweetzyme®.

Lyases

Suitable lyases include Polysaccharide lyases: Pectate lyases (4.2.2.2) and pectin lyases (4.2.2.10), such as those from *Bacillus licheniformis* disclosed in WO 99/27083.

The polymeric molecule

The polymeric molecules coupled to the polypeptide may be any suitable polymeric molecule, including natural and synthetic homo-polymers, such as polyols (*i.e.* poly-OH), polyamines (*i.e.* poly-NH_2) and polycarboxyl acids (*i.e.* poly-COOH), and further hetero-polymers *i.e.* polymers comprising one or more different coupling groups *e.g.* a hydroxyl group and amine groups.

Examples of suitable polymeric molecules include polymeric molecules selected from the group comprising polyalkylene oxides (PAO), such as polyalkylene glycols (PAG), including polyethylene glycols (PEG), methoxypolyethylene glycols (mPEG) and polypropylen glycols, PEG-glycidyl ethers (Epox-PEG), PEG-oxycarbonylimidazole (CDI-PEG), Branced PEGs, poly-vinyl alcohol (PVA), poly-carboxylates, poly-(vinylpyrolidone), poly-D,L-amino acids, polyethylene-co-maleic acid anhydride, polystyrene-co-

malic acid anhydrid, dextrans including carboxymethyl-dextrans, heparin, homologous albumin, celluloses, including methylcellulose, carboxymethylcellulose, ethylcellulose, hydroxyethylcellulose carboxyethylcellulose and hydroxypropylcellulose, hydrolysates of chitosan, starches such as hydroxyethyl-straches and hydroxy propyl-starches, glycogen, agaroses and derivates thereof, guar gum, pullulan, inulin, xanthan gum, carrageenin, pectin, alginic acid hydrolysates and bio-polymers.

Preferred polymeric molecules are non-toxic polymeric molecules such as (m)polyethylene glycol ((m)PEG) which further requires a relatively simple chemistry for its covalently coupling to attachment groups on the enzyme's surface.

Generally seen polyalkylene oxides (PAO), such as polyethylene oxides, such as PEG and especially mPEG, are the preferred polymeric molecules, as these polymeric molecules, in comparison to polysaccharides such as dextran, pullulan and the like, have few reactive groups capable of cross-linking.

Even though all of the above mentioned polymeric molecules may be used according to the invention the methoxypolyethylene glycols (mPEG) may advantageously be used. This arise from the fact that methoxyethylene glycols have only one reactive end capable of conjugating with the enzyme. Consequently, the risk of cross-linking is less pronounced. Further, it makes the product more homogeneous and the reaction of the polymeric molecules with the enzyme easier to control.

An example of a branched PEG conjugate is Branched PEG2-NHS-ester of Lysine (available from Shearwater).

Activation and coupling of polymers to polypeptides

If the polymeric molecules to be conjugated with the polypeptide in question are not active, they must be activated by the use of a suitable technique. It is also contemplated according to the invention to couple the polymeric molecules to the polypeptide through a linker. Suitable linkers are well-known to the skilled person.

Methods and chemistry for activation of polymeric molecules as well as for conjugation of polypeptides are intensively described in the literature. Commonly used methods for activation of insoluble polymers include activation of functional groups with cyanogen bromide, periodate, glutaraldehyde, biepoxides, epichlorohydrin, divinylsulfone, carbodiimide, sulfonyl halides, trichlorotriazine etc. (see R.F. Taylor, (1991), "Protein immobilisation. Fundamental and applications", Marcel Dekker, N.Y.; S.S. Wong, (1992), "Chemistry of Protein Conjugation and Crosslinking", CRC Press, Boca Raton; G.T. Hermanson et al., (1993), "Immobilized Affinity Ligand Techniques", Academic Press, N.Y.). Some of the methods concern activation of insoluble polymers but are also applicable to activation of soluble polymers *e.g.* periodate, trichlorotriazine, sulfonylhalides, divinylsulfone, carbodiimide etc. The functional groups being amino, hydroxyl, thiol, carboxyl, aldehyde or sulfydryl on the polymer and the chosen attachment group on the protein must be considered in choosing the activation and conjugation chemistry which normally consist of i) activation of polymer, ii) conjugation, and iii) blocking of residual active groups.

In the following a number of suitable polymer activation methods will be described shortly. However, it is to be understood that also other methods may be used.

Coupling polymeric molecules to the free acid groups of polypeptides may be performed with the aid of diimide and for example amino-PEG or hydrazino-PEG (Pollak et al., (1976), J. Amr. Chem. Soc., 98, 289-291) or diazoacetate/amide (Wong et al., (1992), "Chemistry of Protein Conjugation and Crosslinking", CRC Press).

Coupling polymeric molecules to hydroxy groups are generally very difficult as it must be performed in water. Usually hydrolysis predominates over reaction with hydroxyl groups.

Coupling polymeric molecules to free sulfhydryl groups can be reached with special groups like maleimido or the *ortho*-pyridyl disulfide. Also vinylsulfone (US patent no. 5,414,135, (1995), Snow et al.) has a preference for sulfhydryl groups but is not as selective as the other mentioned.

Accessible Arginine residues in the polypeptide chain may be targeted by groups comprising two vicinal carbonyl groups.

Techniques involving coupling electrophilically activated PEGs to the amino groups of Lysines may also be useful. Many of the usual leaving groups for alcohols give rise to an amine linkage. For instance, alkyl sulfonates, such as tresylates (Nilsson et al., (1984), Methods in Enzymology vol. 104, Jacoby, W. B., Ed., Academic Press: Orlando, p. 56-66; Nilsson et al., (1987), Methods in Enzymology vol. 135; Mosbach, K., Ed.; Academic Press: Orlando, pp. 65-79; Scouten et al., (1987), Methods in Enzymology vol. 135, Mosbach, K., Ed., Academic Press: Orlando, 1987; pp 79-84; Crossland et al., (1971), J. Amr. Chem. Soc. 1971, 93, pp. 4217-4219), mesylates (Harris, (1985), supra; Harris et al., (1984), J. Polym. Sci. Polym. Chem. Ed. 22, pp 341-352), aryl sulfonates like tosylates, and *para*-nitrobenzene sulfonates can be used.

Organic sulfonyl chlorides, *e.g.* Tresyl chloride, effectively converts hydroxy groups in a number of polymers, *e.g.* PEG, into good leaving groups (sulfonates) that, when reacted with nucleophiles like amino groups in polypeptides allow stable linkages to be formed between polymer and polypeptide. In addition to high conjugation yields, the reaction conditions are in general mild (neutral or slightly alkaline pH, to avoid denaturation and little or no disruption of activity), and satisfy the non-destructive requirements to the polypeptide.

Tosylate is more reactive than the mesylate but also more unstable decomposing into PEG, dioxane, and sulfonic acid (Zalipsky, (1995), Bioconjugate Chem., 6, 150-165). Epoxides may also been used for creating amine bonds but are much less reactive than the above mentioned groups.

Converting PEG into a chloroformate with phosgene gives rise to carbamate linkages to Lysines. This theme can be played in many variants substituting the chlorine with N-hydroxy succinimide (US patent no. 5,122,614, (1992); Zalipsky et al., (1992), Biotechnol. Appl. Biochem., 15, p. 100-114; Monfardini et al., (1995), Bioconjugate Chem., 6, 62-69, with imidazole (Allen et al., (1991), Carbohydr. Res., 213, pp 309-319), with

para-nitrophenol, DMAP (EP 632 082 A1, (1993), Looze, Y.) etc. The derivatives are usually made by reacting the chloroformate with the desired leaving group. All these groups give rise to carbamate linkages to the peptide.

Furthermore, isocyanates and isothiocyanates may be employed yielding ureas and thioureas, respectively.

Amides may be obtained from PEG acids using the same leaving groups as mentioned above and cyclic imid thrones (US patent no. 5,349,001, (1994), Greenwald et al.). The reactivity of these compounds are very high but may make the hydrolysis to fast.

PEG succinate made from reaction with succinic anhydride can also be used. The hereby comprised ester group make the conjugate much more susceptible to hydrolysis (US patent no. 5,122,614, (1992), Zalipsky). This group may be activated with N-hydroxy succinimide.

Furthermore, a special linker can be introduced. The most commonly used is cyanuric chloride (Abuchowski et al., (1977), J. Biol. Chem., 252, 3578-3581; US patent no. 4,179,337, (1979), Davis et al.; Shafer et al., (1986), J. Polym. Sci. Polym. Chem. Ed., 24, 375-378.

Coupling of PEG to an aromatic amine followed by diazotation yields a very reactive diazonium salt which *in situ* can be reacted with a peptide. An amide linkage may also be obtained by reacting an azlactone derivative of PEG (US patent no. 5,321,095, (1994), Greenwald, R. B.) thus introducing an additional amide linkage.

As some peptides do not comprise many Lysines it may be advantageous to attach more than one PEG to the same Lysine. This can be done *e.g.* by the use of 1,3-diamino-2-propanol.

PEGs may also be attached to the amino-groups of the enzyme with carbamate linkages (WO 95/11924, Greenwald et al.). Lysine residues may also be used as the backbone.

The coupling technique used in the examples is the N-succinimidyl carbonate conjugation technique descried in WO 90/13590 (Enzon).

Method for preparing improved polypeptides

It is also an object of the invention to provide a method for preparing improved polypeptides comprising the steps of:

a) identifying amino acid residues located on the surface of the 3-dimensional structure of the parent polypeptide in question,

b) selecting target amino acid residues on the surface of said 3-dimensional structure of said parent polypeptide to be modified,

c) substituting one or more amino acid residues selected in step b) with other amino acid residue, and/or

d) coupling polymeric molecules to the amino acid residues in step b) and/or step c).

Step a) Identifying amino acid residues located on the surface of the parent polypeptide

3-dimensional structure

To perform the method of the invention a 3-dimensional structure of the parent polypeptide in question is required. This structure may for example be an X-ray structure, an NMR structure or a model-built structure. The Brookhaven Databank is a source of X-ray- and NMR-structures.

A model-built structure may be produced by the person skilled in the art if one or more 3-dimensional structure(s) exist(s) of homologous polypeptide(s) sharing at least 30% sequence identity with the polypeptide in question. Several software packages exist which may be employed to construct a model structure. One example is the Homology 95.0 package from MSI Inc.

Typical actions required for the construction of a model structure are: alignment of homologous sequences for which 3-dimensional structures exist, definition of Structurally Conserved Regions (SCRs), assignment of coordinates to SCRs, search for structural fragments/loops in structure databases to replace Variable Regions, assignment of coordinates to these regions, and structural refinement by energy minimization. Regions containing large inserts (≥3 residues) relative to the known 3-dimensional structures are known to be quite difficult

to model, and structural predictions must be considered with care.

Having obtained the 3-dimensional structure of the polypeptide in question, or a model of the structure based on homology to known structures, this structure serves as an essential prerequisite for the fulfillment of the method described below.

Step b) Selection of target amino acid residues

Target amino acid residues to be modified are according to the invention selected from those amino acid residues, wherein the C^{α}-atom is located less than 15 Å from a ligand. In a preferred embodiment a possible C^{β}-atom should be closer to the ligand than the C^{α}-atom. In a more preferred embodiment the C^{α}-atom of the amino acid residue is located less than 10 Å from the ligand and said amino acid residues have an accessibility of at least 15%, preferably at least 20% and more preferably at least 30%.

Step c) Substitution

Conservative substitution

It is preferred to make conservative substitutions in the polypeptide when the polypeptide has to be conjugated, as conservative substitutions secure that the impact of the substitution on the polypeptide structure is limited.

In the case of providing additional amino groups this may be done by substitution of Arginine to Lysine, both residues being positively charged, but only the Lysine having a free amino group suitable as an attachment groups.

In the case of providing additional carboxylic acid groups the conservative substitution may for instance be an Asparagine to Aspartic acid or Glutamine to Glutamic acid substitution. These residues resemble each other in size and shape, except from the carboxylic groups being present on the acidic residues.

In the case of providing SH-groups the conservative substitution may be done by substitution of Threonine or Serine to Cysteine.

Which amino acids to substitute depends in principle on the coupling chemistry to be applied.

When no coupling is performed after substitution there is in general no limit on the selection of amino acids for substitution. However, preferred amino acids for substitutions are substitutions to polar residues e.g. K, R, D, E, H, Q, N, S, T, C. Also substitutions to residues with short side chains G and A are preferred.

Further, when no coupling is to be performed, the changes may be in the form of addition or deletion of at least one amino acid for which the C^{α} atom is located within 15Å from the bound ligand, preferably deleting an amino acid. Furthermore, the parent protein may be changed by substituting some amino acids and deleting/adding other.

Only substitutions which provide polypeptides with reduced immune response when evaluated in animal models are within the concept of the present invention.

The mutation(s) performed in step c) may be performed by standard techniques well known in the art, such as site-directed mutagenesis (see, *e.g.*, Sambrook et al. (1989), Molecular Cloning. A Laboratory Manual, Cold Spring Harbor, NY.

A general description of nucleotide substitution can be found in e.g. Ford *et al.*, 1991, *Protein Expression and Purification* 2, p. 95-107.

In a preferred embodiment of the invention, more than one amino acid residue is substituted, added or deleted, these amino acids possibly being located close to different bound ligands. In that case, it may be difficult to assess a priori how well the functionality of the protein is maintained while antigenicity, immunogenicity and/or allergenicity is reduced. This can be achieved by establishing a library of diversified mutants each having one or more changed amino acids introduced and selecting those variants which show good retention of function and at the same time a good reduction in antigenicity. In the case of protease, this can be tested by assaying the

secreted variants for enzyme activity (as described below in the experimental section) and for antigen binding (e.g. by competitive ELISA using methods known in the art. (see e.g J. Clausen, Immunochemical Techniques For The Identification and Estimation of Macromolecules, Elsevier, Amsterdam, 1988 pp.187-188). Specifically, the competivity ELISA can be performed with the wild-type protease coated on ELISA plates, and incubated with specific polyclonal anti-protease antiserum from rabbits in the presence of protease variant. The scope of these embodiments of the invention is by no means limited to protease, which serves only to provide an example. A diversified library can be established by a range of techniques known to the person skilled in the art (Reetz MT; Jaeger KE, in Biocatalysis - from Discovery to Application edited by Fessner WD, Vol. 200, pp. 31-57 (1999); Stemmer, Nature, vol. 370, p.389-391, 1994; Zhao and Arnold, Proc. Natl. Acad. Sci., USA, vol. 94, pp. 7997-8000, 1997; or Yano et al., Proc. Natl. Acad. Sci., USA, vol. 95, pp 5511-5515, 1998). In a more preferable embodiment, substitutions are found by a method comprising the following steps: 1) a range of substitutions, additions, and/or deletions are listed, 2) a library is designed which introduces a randomized subset of these changes in the amino acid sequence into the target gene, e.g. by random mutagenesis, 3) the library is expressed, and preferred variants are selected. In a most preferred embodiment, this method is supplemented with additonal rounds of screening and/or family shuffling of hits from the first round of screening (J.E. Ness, et al, Nature Biotechnology, vol. 17, pp. 893-896, 1999) and/or combination with other methods of reducing allergenicity by genetic means (such as that disclosed in WO92/10755).

Generation of site directed mutations

Prior to mutagenesis the gene encoding the polypeptide of interest must be cloned in a suitable vector. Methods for generating mutations in specific sites is described below.

Once the polypeptide-encoding gene has been cloned, desirable sites for mutation identified, and the residue(s) to

substitute for the original one(s) have been decided, these mutations can be introduced using synthetic oligonucleotides. These oligonucleotides contain nucleotide sequences flanking the desired mutation sites; mutant nucleotides are inserted during oligo-nucleotide synthesis. In a preferred method, Site-directed mutagenesis is carried out by SOE-PCR mutagenesis technique described by Kammann et al. (1989) Nucleic Acids Research 17(13), 5404, and by Sarkar G. and Sommer, S.S. (1990); Biotechniques 8, 404-407.

Step d) Coupling polymeric molecules to the optionally modified parent enzyme

Polypeptide-polymer conjugates of the invention may be prepared by any coupling method known in the art including the above mentioned techniques.

Preparation of enzyme variants

Enzyme variants to be conjugated may be constructed by any suitable method. A number of methods are well established in the art. For instance enzyme variants according to the invention may be generated using the same materials and methods described in e.g. WO 89/06279 (Novo Nordisk A/S), EP 130,756 (Genentech), EP 479,870 (Novo Nordisk A/S), EP 214,435 (Henkel), WO 87/04461 (Amgen), WO 87/05050 (Genex), EP application no. 87303761 (Genentech), EP 260,105 (Genencor), WO 88/06624 (Gist-Brocades NV), WO 88/07578 (Genentech), WO 88/08028 (Genex), WO 88/08033 (Amgen), WO 88/08164 (Genex), Thomas et al. (1985) Nature, **318** 375-376; Thomas et al. (1987) J. Mol. Biol., 193, 803-813; Russel and Fersht (1987) Nature **328** 496-500.

Coupling of polymeric molecules to the polypeptide in question

See previous paragraphs

Immunogenicity and Allergenicity

"Immunogenicity" is a wider term than "antigenicity" and "allergenicity", and expresses the immune system's response to the presence of foreign substances. Said foreign substances are

called immunogens, antigens and allergens depending of the type of immune response the elicit.

An "immunogen" may be defined as a substance which, when introduced into circulatory system of animals and humans, is capable of stimulating an immunologic response resulting in formation of immunoglobulin.

The term "antigen" refers to substances which by themselves are capable of generating antibodies when recognized as a non-self molecule.

Further, an "allergen" may be defined as an antigen which may give rise to allergic sensitization or an allergic response by IgE antibodies (in humans, and molecules with comparable effects in animals).

Assessment of immunogencity

Assessment of the immunogenicity may be made by injecting animal subcutaneously to enter the immunogen into the circulation system and comparing the response with the response of the corresponding parent polypeptide.

The "circulatory system" of the body of humans and animals means, in the context of the present invention, the system which mainly consists of the heart and blood vessels. The heart delivers the necessary energy for maintaining blood circulation in the vascular system. The circulation system functions as the organism's transportation system, when the blood transports O_2, nutritious matter, hormones, and other substances of importance for the cell regulation into the tissue. Further the blood removes CO_2 from the tissue to the lungs and residual substances to *e.g.* the kidneys. Furthermore, the blood is of importance for the temperature regulation and the defence mechanisms of the body, which include the immune system.

A number of *in vivo* animal models exist for assessment of the immunogenic potential of polypeptides. Some of these models give a suitable basis for hazard assessment in man. Suitable models include a mice model.

This model seek to identify the immunogenic response in the form of the IgG response in Balb/C mice being injected subcutaneously with modified and unmodified polypeptides.

Also other animal models can be used for assessment of the immunogenic potential.

A polypeptide having "reduced immunogenicity" according to the invention indicates that the amount of produced antibodies, *e.g.* immunoglobulin in humans, and molecules with comparable effects in specific animals, which can lead to an immune response, is significantly decreased, when introduced into the circulatory system, in comparison to the corresponding parent polypeptide.

For Balb/C mice the IgG response gives a good indication of the immunigenic potential of polypeptides.

Assessment of allergenicity

Assessment of allergenicity may be made by inhalation tests, comparing the effect of intratracheally (into the trachea) administrated parent enzymes with the corresponding modified enzymes according to the invention.

A number of *in vivo* animal models exist for assessment of the allegenicity of enzymes. Some of these models give a suitable basis for hazard assessment in man. Suitable models include a guinea pig model and a mouse model. These models seek to identify respiratory allergens as a function of elicitation reactions induced in previously sensitised animals. According to these models the alleged allergens are introduced intratracheally into the animals.

A suitable strain of guinea pigs, the Dunkin Hartley strain, do not as humans, produce IgE antibodies in connection with the allergic response. However, they produce another type of antibody the IgG1A and IgG1B (see *e.g.* Prentø, ATLA, 19, p. 8-14, 1991), which are responsible for their allergenic response to inhaled polypeptides including enzymes. Therefore, when using the Dunkin Hartley animal model, the relative amount of IgG1A and IgG1B is a measure of the allergenicity level.

The Balb/C mice strain is suitable for intratracheal, intredermal or subcutaneous exposure. Balb/C mice produce IgE as the allergic response.

More details on assessing respiratory allergens in guinea pigs and mice is described by Kimber et al.,(1996), Fundamental and

Applied Toxicology, 33, p. 1-10.

Other animals such as rats, rabbits etc. may also be used for comparable studies.

Composition

The invention relates to a composition comprising a modified polypeptide of the invention.

The composition may be a pharmaceutical or industrial composition.

The composition may further comprise other polypeptides, proteins or enzymes and/or ingredients normally used in *e.g.* detergents, including soap bars, household articles, agrochemicals, personal care products, including skin care compositions, cleaning compositions for *e.g.* contact lenses, oral and dermal pharmaceuticals, composition use for treating textiles, compositions used for manufacturing food, *e.g.* baking, and food/feed etc.

Use of the polypeptide

The invention also relates to the use of the method of the invention for reducing the immune response of polypeptides.

It is also an object of the invention to use the polypeptide-polymer conjugate or the polypeptide otherwise modified according to the invention to reduce the allergenicity of industrial products, such as detergents, such as laundry, disk wash and hard surface cleaning detergents, food or feed products, personal care products and textile products.

MATERIAL AND METHODS

Materials

Enzymes:

PD498: Protease of subtilisin type shown in WO 93/24623. The sequence of PD498 is shown in SEQ ID NO. 1 and 2.

Savinase®: The sequence is shown in SEQ ID NO 3 (Available from Novo Nordisk A/S)

Subtilisin BPN´: The sequence can be found in the SWISS-PROT database. The sequence is also disclosed in:

GALLAGHER T., OLIVER J., BOTT R., BETZEL C., GILLILAND G.L.; "Subtilisin BPN' at 1.6-A resolution: analysis for discrete disorder and comparison of crystal forms."; Acta Crystallogr. D 52:1125-1135(1996). The enzyme is available from Novo Nordisk A/S.

Amylase AA560: The alkaline α-amylase may be derived from a strain of Bacillus sp. DSM 12649. The strain was deposited on 25th January 1999 by the inventors under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure at Deutshe Sammmlung von Microorganismen und Zellkulturen GmbH (DSMZ), Mascheroder Weg 1b, D-38124 Braunschweig DE.The sequence is shown in SEQ ID NO. 4.

Strains:

B. subtilis 309 and 147 are variants of *Bacillus lentus*, deposited with the NCIB and accorded the accession numbers NCIB 10309 and 10147, and described in US Patent No. 3,723,250 incorporated by reference herein.

E. coli MC 1000 (M.J. Casadaban and S.N. Cohen (1980); *J. Mol. Biol.* **138** 179-207), was made r^-,m^+ by conventional methods and is also described in US Patent Application Serial No. 039,298.

Vectors:

pPD498: *E. coli* - *B. subtilis* shuttle vector (described in US patent No. 5,621,089 under section 6.2.1.6) containing the wild-type gene encoding for PD498 protease (SEQ ID NO. 2). The same vector is use for mutagenesis in *E. coli* as well as for expression in *B. subtilis*.

Materials, chemicals and solutions:

Horse Radish Peroxidase labeled anti-rat-Ig (Dako, DK, P162, # 031; dilution 1:1000).

Mouse anti-rat IgE (Serotec MCA193; dilution 1:200).
Rat anti-mouse IgE (Serotec MCA419; dilution 1:100).
Biotin-labeled mouse anti-rat IgG1 monoclonal antibody (Zymed 03-9140; dilution 1:1000)
Biotin-labeled rat anti-mouse IgG1 monoclonal antibody (Serotec MCA336B; dilution 1:1000)
Streptavidin-horse radish peroxidase (Kirkegård & Perry 14-30-00; dilution 1:1000).
CovaLink NH_2 plates (Nunc, Cat# 459439)
Cyanuric chloride (Aldrich)
Acetone (Merck)
Rat anti-Mouse IgG1, biotin (SeroTec, Cat# MCA336B)
Streptavidin, peroxidase (KPL)
Ortho-Phenylene-diamine (OPD) (Kem-en-Tec, Cat# 4260)
H_2O_2, 30% (Merck)
Tween 20 (Merck)
Skim Milk powder (Difco)
H_2SO_4 (Merck)

Buffers and Solutions:

Carbonate buffer (0.1 M, pH 10 (1 liter))	Na_2CO_3	10.60 g
PBS (pH 7.2 (1 liter))	NaCl	8.00 g
	KCl	0.20 g
	K_2HPO_4	1.04 g
	KH_2PO_4	0.32 g

Washing buffer PBS, 0.05% (v/v) Tween 20
Blocking buffer PBS, 2% (wt/v) Skim Milk powder
Dilution buffer PBS, 0.05% (v/v) Tween 20, 0.5% (wt/v) Skim Milk powder

Citrate buffer (0.1M, pH 5.0-5.2 (1 liter))	NaCitrate	20.60 g
	Citric acid	6.30 g

Sodium Borate, borax (Sigma)
3,3-Dimethyl glutaric acid (Sigma)
$CaCl_2$ (Sigma)
Tresyl chloride (2,2,2-triflouroethansulfonyl chloride) (Fluka)
1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) (Fluka)
N-Hydroxy succinimide (Fluka art. 56480))

Phosgene (Fluka art. 79380)
Lactose (Merck 7656)
PMSF (phenyl methyl sulfonyl flouride) from Sigma
Succinyl-Alanine-Alanine-Proline-Phenylalanine-para-nitroanilide (Suc-AAPF-pNP) Sigma no. S-7388, Mw 624.6 g/mole.

Activation of CovaLink plates:

· Make a fresh stock solution of 10 mg cyanuric chloride per ml acetone.
· Just before use, dilute the cyanuric chloride stock solution into PBS, while stirring, to a final concentration of 1mg/ml.
· Add 100 ml of the dilution to each well of the CovaLink NH2 plates, and incubate for 5 minutes at room temperature.
· Wash 3 times with PBS.
· Dry the freshly prepared activated plates at 50°C for 30 minutes.
· Immediately seal each plate with sealing tape.
· Preactivated plates can be stored at room temperature for 3 weeks when kept in a plastic bag.

Test Animals:

Female Balb/C mice (about 20 grams) purchased from Bomholdtgaard, Ry, Denmark.
Female Brown-Norway rats, weighing on the average 180 g

Equipment:

XCEL II (Novex)
ELISA reader (UVmax, Molecular Devices)
HPLC (Waters)
PFLC (Pharmacia)
Superdex-75 column, Mono-Q, Mono S from Pharmacia, SW.
SLT: Fotometer from SLT LabInstruments
Size-exclusion chromatograph (Spherogel TSK-G2000 SW).
Size-exclusion chromatograph (Superdex 200, Pharmacia, SW)
Amicon Cell

Enzymes for DNA manipulations

Unless otherwise mentioned all enzymes for DNA manipulations, such as *e.g.* restriction endonucleases, ligases etc., are obtained from New England Biolabs. Inc.

Media:

BPX: Composition (per liter)

Potato starch	100g
Ground barley	50g
Soybean flour	20g
Na_2HPO_4 X 12 H_2O	9g
Pluronic	0.1g
Sodium caseinate	10g

The starch in the medium is liquefied with α-amylase and the medium is sterilized by heating at 120°C for 45 minutes. After sterilization the pH of the medium is adjusted to 9 by addition of $NaHCO_3$ to 0.1 M.

Methods

General molecular biology methods:

Unless otherwise mentioned the DNA manipulations and transformations were performed using standard methods of molecular biology (Sambrook et al. (1989) Molecular cloning: A laboratory manual, Cold Spring Harbor lab., Cold Spring Harbor, NY; Ausubel, F. M. et al. (eds.) "Current protocols in Molecular Biology". John Wiley and Sons, 1995; Harwood, C. R., and Cutting, S. M. (eds.) "Molecular Biological Methods for Bacillus". John Wiley and Sons, 1990).
Enzymes for DNA manipulations were used according to the specifications of the suppliers.

Fermentation of PD498 variants

Fermentation of PD498 variants in *B. subtilis* are performed at 30°C on a rotary shaking table (300 r.p.m.) in 500 ml baffled Erlenmeyer flasks containing 100 ml BPX medium for 5 days. In order to make an *e.g.* 2 liter broth 20 Erlenmeyer flasks are fermented simultaneously.

Purification of PD498 variants

Approximately 1.6 litres of PD498 variant fermentation broth are centrifuged at 5000 rpm for 35 minutes in 1 litre beakers. The supernatants are adjusted to pH 7.0 using 10% acetic acid and filtered on Seitz Supra S100 filter plates.
The filtrates are concentrated to approximately 400 ml using an Amicon CH2A UF unit equipped with an Amicon S1Y10 UF cartridge.
The UF concentrate is centrifuged and filtered prior to absorption at room temperature on a Bacitracin affinity column at pH 7. The PD498 variant is eluted from the Bacitracin column at room temperature using 25% 2-propanol and 1 M sodium chloride in a buffer solution with 0.01 dime-thyl-glutaric acid, 0.1 M boric acid and 0.002 M calcium chloride adjusted to pH 7.
The fractions with protease activity from the Bacitracin purification step are combined and applied to a 750 ml Sephadex G25 column (5 cm diameter) equilibrated with a buffer containing 0.01 dimethylglutaric acid, 0.1 M boric acid and 0.002 M calcium chloride adjusted to pH 6.0.
Fractions with proteolytic activity from the Sephadex G25 column are combined and applied to a 150 ml CM Sepharose CL 6B cat-ion exchange column (5 cm diameter) equilibrated with a buffer containing 0.01 M dimethylglutaric acid, 0.1 M boric acid, and 0.002 M calcium chloride adjusted to pH 6.0.
The protease is eluted using a linear gradient of 0-0.5 M sodium chloride in 1 litres of the same buffer.
Protease containing fractions from the CM Sepharose column are combined and filtered through a 2µ filter.

Determination of the molecule weight

Electrophoretic separation of proteins was performed by standard methods using 4-20% gradient SDS poly acrylamide gels (Novex). Proteins were detected by silver staining. The molecule weight was measured relative to the mobility of Mark-12® wide range molecule weight standards from Novex.

Protease activity

Analysis with Suc-Ala-Ala-Pro-Phe-pNa:

Proteases cleave the bond between the peptide and p-nitroaniline to give a visible yellow colour absorbing at 405 nm.

Buffer: *e.g.* Britton and Robinson buffer pH 8.3
Substrate: 100 mg suc-AAPF-pNa is dissolved into 1 ml dimethyl sulfoxide (DMSO). 100 ml of this is diluted into 10 ml with Britton and Robinson buffer.

The substrate and protease solution is mixed and the absorbance is monitored at 405 nm as a function of time and $ABS_{405\ nm}$/min. The temperature should be controlled (20-50°C depending on protease). This is a measure of the protease activity in the sample.

Proteolytic Activity

In the context of this invention proteolytic activity is expressed in Kilo NOVO Protease Units (KNPU). The activity is determined relatively to an enzyme standard (SAVINASE_), and the determination is based on the digestion of a dimethyl casein (DMC) solution by the proteolytic enzyme at standard conditions, *i.e.* 50°C, pH 8.3, 9 min. reaction time, 3 min. measuring time. A folder AF 220/1 is available upon request to Novo Nordisk A/S, Denmark, which folder is hereby included by reference.

A GU is a Glycine Unit, defined as the proteolytic enzyme activity which, under standard conditions, during a 15-minutes' incubation at 40°C, with N-acetyl casein as substrate, produces an amount of NH_2-group equivalent to 1 mmole of glycine.

Enzyme activity can also be measured using the PNA assay, according to reaction with the soluble substrate succinyl-alanine-alanine-proline-phenyl-alanine-para-nitrophenol, which is described in the Journal of American Oil Chemists Society, Rothgeb, T.M., Goodlander, B.D., Garrison, P.H., and Smith, L.A., (1988).

ELISA IgE test system (for Brown Norway rats):

A three layer sandwich ELISA is used to determine relative concentrations of specific antibodies.

The immunizing molecule is used as coating antigen with 10 mg per ml and 50 ml per well, in neutral phosphate buffer, incubated overnight at 4°C. All remaining binding spots on the well surface are blocked in 2 % skim milk, 200 ml per well in phosphate buffer for at least 30 minutes at room temperature (RT). All seras to be tested with this antigen are added at 50 ml per well to this plate using a 8-channel pipette in dilution series from 10 x diluted followed by 3-fold dilutions. Dilutions are made in phosphate buffer with 0.5 % skim milk and 0.05% Tween20, incubated 2 hours on agitation platform at RT. The "tracer" molecule is biotinylated Mouse anti Rat IgE 50 ml per well and diluted 2000 x in phosphate buffer with 0.5 % skim milk and 0.05% Tween 20, incubated 2 hours on an agitation platform at RT. Control (blank) was identical sequence but without rat sera. 50 ml per well streptavidin horse raddish peroxidase, diluted 2000 x was incubated 1 hour on an agitation platform. Colouring substrate at 50 ml per well is OPD (6 mg) and H_2O_2 (4 ml of a 30% solution) per 10 ml citrate buffer pH 5.2. The reaction is stopped using 100 ml per well 2 N H_2SO_4. All readings on SLT at 486 nm and 620 nm as reference. Data is calculated and presented in Lotus.

<u>ELISA procedure to determine relative concentrations of IgE antibodies in BALB/C mice</u>

A three layer sandwich ELISA is used to determine relative concentrations of specific IgE serum antibodies.

1) Coat the ELISA-plate with 10 mg rat anti-mouse IgE or mouse anti-rat IgE/ml buffer 1.

50 ml/well. Incubate over night at 4°C.

2) Empty the plates and block with Blocking buffer at least ½ hour at room temperature.

200 ml/well. Shake gently. Wash the plates 3 times with Washing Buffer.

3) Incubate with mouse/rat sera, starting from undiluted and continue with 2-fold dilutions. Keep some wells free for buffer 4 only (blanks). 50 ml/well. Incubate for 30 minutes at room temperature. Shake gently. Wash the plates 3 times in Washing Buffer.

4) Dilute the enzyme in Dilution buffer to the appropriate protein concentration. 50ml/well.
Incubate for 30 minutes at room temperature. Shake gently. Wash the plates 3 times in Washing Buffer.

5) Dilute specific polyclonal anti-enzyme antiserum serum (pIg) for detecting bound antibody in Dilution buffer. 50ml/well. Incubate for 30 minutes at room temperature. Shake gently. Wash the plates 3 times in Washing Buffer.

6) Dilute Horseradish Peroxidase-conjugated anti-pIg-antibody in Dilution buffer. 50 ml/well.
Incubate at room temperature for 30 minutes. Shake gently. Wash the plates 3 times in Washing Buffer.

7) Mix 0.6 mg ODP/ml + 0.4 µl H_2O_2/ml in substrate Buffer. Make the solution just before use. Incubate for 10 minutes. 50 µl/well.

8)To stop the reaction: add Stop Solution. 50 µl/well.

9) Read the plates at 492 nm with 620 nm as reference.
Data is calculated and presented in Lotus.

EXAMPLES

Example 1

Subtilisin BPN'

In order to identify the residues to be modified, a distance and a directional criteria are applied.

As disclosed earlier residues having their C^{α}-atom closer than 15 Å to a ligand are targets for modification. Preferably, residues having their C^{β}-atom closer to the ligand bound than the C^{α}-atom, thereby allowing a potential side chain to point in the direction of the ligand, are targets for modification.

The relevant distance can easily be measured using e.g. molecular graphics programs like InsightII from Molecular Simulations INC.

Especially surface exposed residues, defined as having

ACC>0 when applying the DSSP program to the relevant protein part of the structure, are targets for modification. The DSSP program is disclosed in W. Kabsch and C. Sander, BIOPOLYMERS 22 (1983) pp. 2577-2637.

In Thomas E. Creighton, PROTEINS; Structure and Molecular Priciples, WH Freeman and Company, NY, ISBN: 0-7167-1566-X (1984) is disclosed a table listing the accessible surface areas of individual amino acid residues. In the table below 15% and 20% accessibility has been determined.

	Total ACC	20% of Total	15% of Total
AA	ÅxÅ	ÅxÅ	ÅxÅ
Ala	115	23,0	17,3
Arg	225	45,0	33,8
Asn	160	32,0	24,0
Asp	150	30,0	22,5
Cys	135	27,0	20,3
Gln	180	36,0	27,0
Glu	190	38,0	28,5
Gly	75	15,0	11,3
His	195	39,0	29,3
Ile	175	35,0	26,3
Leu	170	34,0	25,5
Lys	200	40,0	30,0
Met	185	37,0	27,8
Phe	210	42,0	31,5
Pro	145	29,0	21,8
Ser	115	23,0	17,3
Thr	140	28,0	21,0
Trp	255	51,0	38,3
Tyr	230	46,0	34,5
Val	155	31,0	23,3

When dividing the found accessible surface area (ACC) for each amino acid of the protein with the accessible surface area for that individual amino acid (found in the Creighton table) the accessibility value in percent is obtained.

In order to find residues to modify, the method described above was applied to the X-ray structure of Subtilisin BPN' in complex with the inhibitor CI-2 (entry 2SNI in the Brookhaven Protein Data Bank).

Only the Subtilisin BPN' and the two metal ions in the

structure was used for the analysis. Both ions are calcium ions. They are found in site 1 and site 2.

The results of the analysis are seen in the tables below. The columns shows the distance in Å from the metal ion to the C^{α} and C^{β} as well as the accessibility as determined by DSSP for each residue to modify.

Site 1:

resid	res.no	dist(C^{α})	dist(C^{β})	ACC (ÅxÅ)	ACC (%)
GLY	80	4.40		14	18.67
ASN	77	4.68	4.57	62	38.75
ASP	41	5.14	4.36	0	
GLN	2	5.46	4.64	47	26.11
ALA	74	5.57	5.12	0	
GLY	83	7.80		0	
PRO	86	8.44	7.42	8	
GLY	70	9.04		1	
THR	208	9.38	8.66	0	
HIS	39	10.41	9.97	3	
PRO	5	10.46	10.17	18	12.41
LYS	43	10.62	10.53	137	68.50
TYR	214	10.68	9.62	75	32.61
GLN	206	11.79	11.27	88	48.89
VAL	8	12.42	10.89	2	
THR	22	13.14	12.12	22	15.71
GLY	215	13.52		14	18.67
PRO	14	13.53	13.29	45	31.03
HIS	17	13.64	12.25	28	14.36
THR	66	13.80	13.76	0	
SER	9	14.40	14.22	58	50.43
ALA	13	14.66	13.53	0	
GLY	7	14.74		0	
LEU	90	14.79	13.38	1	
ASP	36	14.87	14.57	20	13.33
GLY	211	14.88		45	60.00

Site 2:

resid	resno	dist(C^{α})	dist(C^{β})	ACC (ÅxÅ)	ACC (%)
GLU	195	4.44	4.28	48	25.26
ALA	176	4.67	3.85	0	
GLY	169	5.16		0	
ASP	197	5.90	5.14	21	14.00
VAL	165	8.35	6.96	6	
ALA	151	8.54	8.04	0	
GLY	166	9.43		14	18.67
GLY	193	9.46		0	
GLY	264	9.63		7	
VAL	149	9.85	9.50	3	
GLY	178	10.74		0	
VAL	139	10.95	9.63	0	
GLY	154	11.31		17	22.67
SER	163	11.34	10.12	29	25.22
ARG	247	11.35	10.32	47	20.89
LYS	265	11.66	11.35	76	38.00
GLN	251	11.74	10.57	26	14.44
SER	191	11.83	11.04	0	
SER	224	12.34	12.02	0	
VAL	143	12.36	10.91	41	26.45
MET	124	12.43	11.71	0	
GLY	127	12.44		61	81.33
SER	260	12.47	12.12	72	62.61
GLY	131	12.69		29	38.67
VAL	227	13.37	11.90	0	
THR	220	13.55	12.34	3	
LEU	250	13.58	12.73	3	
LEU	135	13.60	13.21	6	
GLY	266	13.93		0	
GLY	128	14.04		16	21.33
SER	190	14.12	14.09	0	
ALA	142	14.13	13.36	0	

ILE	122	14.17	13.65	0	
ALA	223	14.44	13.70	0	
ASN	243	14.50	13.94	21	13.13
ALA	200	14.63	14.15	0	

The table below shows functional preferred substitutions in site 1 and 2 of the BPN´. For Gly 80 the substitution G to S/T G to N/Q and G to K/D means that Glycine in position 80 may preferably be substituted with Serine/Threonine or Asparagine/Glutamine or Lysine/Aspartic acid.

SITE1	Subtilisin BPN'		
Gly-80	G to S/T	G to N/Q	G to K/D
Asn-77	N to D/E	N to K/R	N to A/C
Gln-2	Q to D/E	Q to K/R	Q to A/C
Pro-5	P to G/A	P to C/S	P to K/D
Lys-43	K to S/T/C	K to D/E/R	K to Q/N
Tyr-214	Y to N/Q	Y to A/G/C	Y to K/H
Gln-206	Q to D/E	Q to K/R	Q to A/C
Thr-22	T to K/R	T to Q/N/A	T to D/E/C
Gly-215	G to S/T	G to N/Q	G to K/D
Pro-14	P to G/A	P to C/S	P to K/D
Ser-9	S to K/R	S to Q/N/A	S to D/E/C
Gly-211	G to S/T	G to N/Q	G to K/D

SITE2	Subtilisin BPN'		
Glu-195	G to S/T	G to N/Q	G to K/D
Gly-166	G to S/T	G to N/Q	G to K/D
Gly-154	G to S/T	G to N/Q	G to K/D
Ser-163	S to K/R	S to Q/N/A	S to D/E/C
Arg-247	R to K/H	R to Q/N	R to A/C/E
Lys-265	K to S/T/C	K to D/E/R	K to Q/N
Val-143	V to A/G/H	V to Q/E/C	V to T/S/K
Gly-127	G to S/T	G to N/Q	G to K/D
Ser-260	S to K/R	S to Q/N/A	S to D/E/C
Gly-131	G to S/T	G to N/Q	G to K/D
Gly-128	G to S/T	G to N/Q	G to K/D

Example 2

PD498

The 3-dimensional structure of PD 498 as determined by X-ray

crystallography in Brookhaven Protein Data Bank (PDB) format

The sequence which was used to elucidate the three-dimensional structure forming the basis for the present invention consists of the 280 amino acids derived from *Bacillus sp. PD498,* NCIMB No. 40484 as disclosed in sequence ID No. 2.

The structure of PD498 was solved in accordance with the principle for X-ray crystallographic methods given in "X-Ray Structure Determination", Stout, G.K. and Jensen, L.H., John Wiley & Sons, inc. NY, 1989 and "Protein Crystallography" by Blundell, T.L. and Johnson, L.N., Academic Press, London, 1990. The structural coordinates for the solved crystal structure of PD 498 at 2.2 Å resolution using the isomorphous replacement method are given in a standard PDB format (Brookhaven Protein Data Base) in Appendix 1. It is to be understood that Appendix 1 forms part of the present application.

In Appendix 1 the amino acid residues of the enzyme are identified by three-letter amino acid code (capitalized letters).

PD498 has three bound metal ions. Site 1 is equivalent to site 1 in subtilisin BPN' and contains a calcium ion. Site 2 does not have an equivalent in subtilisin BPN' and contains a calcium ion. Site 3 is in the same region as the 2nd site in subtilisin BPN' and does here contain a sodium ion and a monopropylene glycol ligand.

Applying the above method disclosed in example 1 results in:

Site 1:

residue	resno	dist(C^{α})	dist(C^{β})	ACC (ÅxÅ)	ACC (%)
GLY	89	4.26		4	
ASP	5	5.02	3.92	0	
ASP	48	5.10	4.36	0	
ASN	86	5.15	4.73	33	20.63
ALA	82	5.84	4.97	0	
GLY	87	6.05		41	54.67

GLY	92	7.33		0	
TYR	8	7.87	7.12	12	
TYR	7	8.01	7.63	89	38.70
PRO	47	8.13	8.09	59	40.69
PRO	3	8.61	7.55	9	
GLY	78	8.69		0	
THR	213	9.19	8.55	0	
ARG	51	10.39	9.61	162	72.00
HIS	46	10.41	9.93	1	
LYS	52	10.56	9.41	10	
TYR	219	10.74	9.79	56	24.35
ALA	211	11.55	11.03	9	
GLN	12	11.67	10.44	22	12.22
GLY	218	12.00		18	24.00
ALA	10	12.35	12.15	65	56.52
TYR	11	12.46	12.00	121	47.45
VAL	53	13.30	13.18	18	11.61
PRO	15	13.52	12.10	0	
ARG	28	13.77	12.93	103	45.78
ILE	99	14.16	13.16	0	
ASP	43	14.36	14.04	8	
TRP	1	14.43	13.90	71	27.84
GLY	14	14.60		1	
GLY	234	14.85		0	
GLY	29	14.97		13	17.33

Site 2:

resid	resno	dist(C^{α})	dist(C^{β})	ACC (ÅxÅ)	ACC (%)
ASN	65	4.25	4.04	65	40.63
ASP	61	4.98	3.62	88	58.67
ASP	63	5.30	4.43	46	30.67
ASP	58	5.39	3.87	0	
MET	67	5.53	5.42	42	22.70

ILE	60	7.09	6.76	48	27.43
ARG	103	7.67	6.23	4	
GLY	41	8.03		1	
LEU	69	8.99	8.35	114	67.06
GLY	56	10.02		2	
LYS	55	10.15	9.43	115	57.50
ALA	101	11.02	10.20	0	
TYR	44	11.83	11.14	35	15.22
GLY	73	13.18		0	
ASN	45	13.57	13.14	114	71.25
GLY	119	13.62		0	
GLY	111	13.75		36	48.00
GLY	71	13.78		4	
SER	115	13.82	12.77	24	20.87
GLY	109	13.90		32	42.67
THR	74	13.96	13.69	0	
PRO	215	14.41	13.20	30	20.69
VAL	53	14.70	13.64	18	11.61
VAL	37	14.80	14.62	1	

Site 3:

resid	resno	dist(C^{α})	dist(Cβ)	ACC (ÅxÅ)	ACC (%)
ALA	179	4.07	4.05	0	
ALA	181	4.65	4.11	0	
TRP	200	6.65	6.57	46	18.04
ASP	202	6.86	6.02	19	12.67
ALA	160	7.85	7.10	0	
VAL	158	8.84	8.28	0	
THR	170	9.23	8.58	65	46.43
VAL	148	10.12	8.77	0	
LYS	268	10.74	9.64	108	54.00
ARG	250	11.05	10.04	30	13.33
GLY	183	11.15		2	
GLY	198	11.37		8	
TRP	152	11.64	10.35	35	13.73

LEU	133	11.65	10.63	0	
GLU	254	11.66	10.63	15	7.89
GLY	136	11.84		39	52.00
TYR	269	12.12	11.37	45	19.57
GLY	163	12.15		11	14.67
SER	229	12.16	11.65	0	
LEU	144	13.01	12.62	2	
ASN	196	13.01	12.00	1	
VAL	232	13.12	11.71	0	
LEU	131	13.25	12.69	0	
ILE	253	13.27	12.22	1	
ALA	151	13.59	12.87	0	
THR	225	13.88	12.66	1	
ASN	246	14.04	13.33	17	10.63
GLY	270	14.22		0	
ILE	249	14.51	14.36	4	
ALA	228	14.65	14.00	0	
SER	141	14.78	14.70	21	18.26
ALA	236	14.93	13.63	0	

The table below shows the preferred functional substitutions in site 1, 2 and 3 of PD498.

SITE1	PD498		
Asn-86	N to D/E	N to K/R	N to A/C
Gly-87	G to S/T	G to N/Q	G to K/D
Tyr-7	Y to N/Q	Y to A/G/C	Y to K/H
Pro-47	P to G/A	P to C/S	P to K/D
Arg-51	R to K/H	R to Q/N	R to A/C/E
Tyr-219	Y to N/Q	Y to A/G/C	Y to K/H
Gly-218	G to S/T	G to N/Q	G to K/D
Ala-10	A to N/Q	A to K/R	A to D/E
Tyr-11	Y to N/Q	Y to A/G/C	Y to K/H
Arg-28	R to K/H	R to Q/N	R to A/C/E
Trp-1	W to N/Q	W to A/G/C	W to K/H
Gly-29	G to S/T	G to N/Q	G to K/D

SITE2	PD 498		
Asn-65	N to D/E	N to K/R	N to A/C
Asp-61	D to N/Q	D to K/H	D to A/G/C
Asp-63	D to N/Q	D to K/H	D to A/G/C
Met-67	M to A/G/H	M to Q/E/C	M to T/S/K
Ile-60	I to A/G/H	I to Q/E/C	I to T/S/K
Leu-69	L to A/G/H	L to Q/E/C	L to T/S/K
Lys-55	K to S/T/C	K to D/E/R	K to Q/N
Tyr-44	Y to N/Q	Y to A/G/C	Y to K/H
Asn-45	N to D/E	N to K/R	N to A/C
Gly-111	G to S/T	G to N/Q	G to K/D
Ser-115	S to K/R	S to Q/N/A	S to D/E/C
Gly-109	G to S/T	G to N/Q	G to K/D
Pro-215	P to G/A	P to C/S	P to K/D

SITE3	PD498		
Trp-200	W to N/Q	W to A/G/C	W to K/H
Thr-170	T to K/R	T to Q/N/A	T to D/E/C
Lys-268	K to S/T/C	K to D/E/R	K to Q/N
Gly-136	G to S/T	G to N/Q	G to K/D
Tyr-269	Y to N/Q	Y to A/G/C	Y to K/H
Ser-141	S to K/R	S to Q/N/A	S to D/E/C

Example 3

Savinase

For this example the X-ray structure entry 1SVN in the Brookhaven Protein Data Bank was used. This structure contains two metal ions. Site 1 contains a calcium ion and is at a position equivalent to site 1 in subtilisin BPN'. Site 2 contains a calcium ion at a position equivalent to site 2 in subtilisin BPN'. In the following list a SEQUENTIAL numbering have been applied and NOT the numbering system used in the structure file.

Site 1:

resid	resno	dist(C^{α})	dist(C^{β})	ACC (ÅxÅ)	ACC (%)

GLY	78	4.28		14	18.67
ASN	75	4.74	4.64	61	38.13
ASP	40	5.08	4.34	0	
GLN	2	5.39	4.59	45	25.0
ALA	72	5.49	4.99	0	
GLY	81	7.68		0	
PRO	84	8.28	7.29	5	
GLY	68	8.88		1	
THR	202	9.19	8.67	0	
HIS	38	10.40	9.89	13	
PRO	5	10.47	10.26	14	9.66
ASN	42	10.55	10.50	94	58.75
TYR	208	10.72	9.76	65	28.26
GLN	200	11.75	11.39	82	45.56
ILE	8	12.10	10.58	3	
PRO	14	12.91	12.63	49	33.79
THR	22	13.01	12.24	29	20.71
HIS	17	13.44	12.07	29	14.87
ALA	13	13.78	12.63	0	
GLY	7	14.60		2	
LEU	88	14.86	13.68	0	
GLY	223	14.89		0	
GLY	23	14.93		0	

Site 2:

resid	resno	dist(C^{α})	dist(C^{β})	ACC (ÅxÅ)	ACC (%)
ALA	170	4.88	4.24	0	
GLY	189	5.10		46	61.33
ASP	191	7.22	6.52	6	
ALA	149	7.79	7.05	0	
ILE	159	8.29	6.89	1	
VAL	147	8.98	8.40	0	
VAL	137	9.81	8.44	0	
GLY	187	10.71		3	
GLY	258	10.85		3	

ARG	241	10.90	9.77	39	17.33
GLY	172	11.27		0	
GLY	125	11.66		46	61.33
THR	141	11.72	10.47	20	14.29
LEU	122	11.73	10.70	0	
GLY	152	11.96		8	
LEU	133	12.29	11.70	3	
GLN	185	12.41	11.63	14	7.74
THR	218	12.51	11.95	0	
LYS	245	12.79	11.71	48	24.00
SER	259	12.93	12.67	35	30.43
ASN	237	13.34	12.53	22	13.75
ALA	120	13.49	13.00	0	
THR	254	13.53	13.19	100	71.43
VAL	221	13.62	12.14	0	
ALA	140	13.65	13.13	0	
VAL	145	13.91	13.88	0	
THR	214	14.00	12.84	2	
GLY	157	14.11		42	56.00
LEU	244	14.27	13.26	0	
ALA	217	14.97	14.17	0	

The table below shows the preferred functional substitutions in site 1 and 2 of Savinase.

SITE1	Savinase		
Gly-78	G to S/T	G to N/Q	G to K/D
Asn-75	N to D/E	N to K/R	N to A/C
Gln-2	Q to D/E	Q to K/R	Q to A/C
Asn-42	N to D/E	N to K/R	N to A/C
Tyr-208	Y to N/Q	Y to A/G/C	Y to K/H
Gln-200	Q to D/E	Q to K/R	Q to A/C
Pro-14	P to G/A	P to C/S	P to K/D
Thr-22	T to K/R	T to Q/N/A	T to D/E/C
His-17	H to S/T/C	H to D/E	H to Q/N

SITE2	Savinase		
Gly-189	G to S/T	G to N/Q	G to K/D
Arg-241	R to K/H	R to Q/N	R to A/C/E
Gly-125	G to S/T	G to N/Q	G to K/D
Lys-245	K to S/T/C	K to D/E/R	K to Q/N
Ser-259	S to K/R	S to Q/N/A	S to D/E/C
Thr-254	T to K/R	T to Q/N/A	T to D/E/C
Gly-157	G to S/T	G to N/Q	G to K/D

Example 4

Amylase (AA560)

For this example the structure of AA560 has been found by homology modelling using the BAN/Termamyl α-amylase structure disclosed in WO 96/23874 which is hereby incorporated by reference. This structure contains two metal ions. Both site 1 and 2 contain a calcium ion.

The example shows how a 3-dimensional structure determined by model building using coordinates from a homologous structure, can be used to identify residues of the ligand binding site, which may be modified in order to reduce the immune response.

Applying the method disclosed above results in:

Site 1:

Res	ACC (ÅxÅ)	ACC ()
TYR 58:CA	23	10.00
GLY 59:CA	4	
ALA 60:CA	0	
VAL 103:CA	0	
VAL 104:CA	1	
MET 105:CA	6	
ASN 106:CA	1	
HIS 107:CA	6	
LYS 108:CA	14	
GLY 109:CA	2	
VAL 122:CA	3	
PRO 124:CA	27	18.62
ASN 126:CA	28	17.50

ARG 127:CA	17	
ASN 128:CA	107	66.88
THR 141:CA	0	
TRP 159:CA	75	29.41
TYR 160:CA	96	41.74
HIS 161:CA	2	
PHE 162:CA	0	
ASP 163:CA	1	
GLY 164:CA	0	
VAL 165:CA	6	
ASP 166:CA5	64	42.67
ILE 177:CA	12	
TYR 178:CA	0	
LYS 179:CA	27	13.50
PHE 180:CA	0	
LYS 185:CA	36	18.00
GLY 186:CA	24	32.00
TRP 187:CA	27	10.59
ASP 188:CA	0	
TRP 189:CA	136	53.33
GLU 190:CA	39	20.53
VAL 191:CA	0	
ASP 192:CA	11	
THR 193:CA	84	60.00
GLU 194:CA	88	46.32
ASN 195:CA	36	22.50
GLY 196:CA	27	36.00
ASN 197:CA	8	
TYR 198:CA	41	17.83
ASP 199:CA	1	
TYR 200:CA	2	
LEU 201:CA	50	29.41
MET 202:CA	72	38.92
TYR 203:CA	93	40.43
ALA 204:CA	2	
ASP 205:CA	0	
ILE 206:CA	4	
ASP 207:CA	6	
MET 208:CA	5	
ASP 209:CA	74	49.33
HIS 210:CA	39	20.00
VAL 213:CA	0	
VAL 214:CA	26	16.77
LEU 217:CA	4	
ILE 235:CA	0	
ASP 236:CA	15	
ALA 237:CA	5	
VAL 238:CA	0	
LYS 239:CA	14	
HIS 240:CA	13	
ILE 241:CA	1	

LYS 242:CA	44	22.00
TYR 243:CA	5	
SER 244:CA	40	34.78
PHE 245:CA	10	
THR 246:CA	0	
ARG 247:CA	60	26.67
TRP 249:CA	0	
ALA 265:CA	0	
GLU 266:CA	17	8.95
PHE 267:CA	2	
TRP 268:CA	27	10.59

site 2:

Res	ACC (ÅxÅ)	ACC ()
ASN 296: CA	25	15.63
LEU 297: CA	1	
TYR 298: CA	68	29.57
ASN 299: CA	72	45.00
ALA 300: CA	0	
SER 301: CA	0	
LYS 302: CA	117	58.50
SER 303: CA	43	37.39
GLY 304: CA	70	93.33
GLY 305: CA	8	10.67
ASN 306: CA	149	93.13
TYR 307: CA	49	21.30
ASP 308: CA	59	39.33
MET 309: CA	0	
ARG 310: CA	143	63.56
GLN 311: CA	99	55.00
ILE 312: CA	3	
PHE 313: CA	17	8.10
ASN 314: CA	76	47.50
GLU 345: CA	73	38.42
TRP 347: CA	89	38.70
PHE 348: CA	2	
LEU 351: CA	2	
ALA 352: CA	0	
TYR 404: CA	32	13.91
LEU 405: CA	35	20.59
ASP 406: CA	78	52.00
HIS 407: CA	69	35.38
HIS 408: CA	100	51.28
ASN 409: CA	31	19.38
ILE 410: CA	19	10.86
ILE 411: CA	0	
GLY 412: CA	0	
ILE 429: CA	0	

MET 430: CA	5	
SER 431: CA	0	
ASP 432: CA	5	
GLY 433: CA	19	25.33
ALA 434: CA	73	63.48
GLY 435: CA	35	46.67
GLY 436: CA	21	28.00
ASN 437: CA	86	53.75
VAL 474: CA	0	
ASN 475: CA	53	33.13
GLY 476: CA	41	54.67
GLY 477: CA	29	38.67
SER 478: CA	18	15.65
VAL 479: CA	2	

The table below shows functional preferred substitutions in site 1 and 2 of the amylase AA560. For ASN 126 the substitution N to D/E means that Asparagine in position 126 may preferably be substituted with Aspartic acid or Glutamic acid, Lysine or Arginine, or Alanine or Cysteine.

Funtional preferred substitutions								
Site 1					Site 2			
ASN 126	N to D/E	N to K/R	N to A/C		LYS 302	K to S/T/C	K to D/E	K to Q/N
ASN 128	N to D/E	N to K/R	N to A/C		SER 303	S to K/R	S to Q/N/A	S to D/E/C
TRP 159	W to N/Q	W to A/G/C	W to K/H		ASN 306	N to D/E	N to K/R	N to A/C
TYR 160	Y to N/Q	Y to A/G/C	Y to K/H		TYR 307	Y to N/Q	Y to A/G/C	Y to K/H
ASP 166	D to N/Q	D to K/H	D to A/G/C		ASP 308	D to N/Q	D to K/H	D to A/G/C
LYS 185	K to S/T/C	K to D/E	K to Q/N		ARG 310	R to K/H	R to Q/N	R to A/C/E
TRP 189	W to N/Q	W to A/G/C	W to K/H		GLN 311	Q to D/E	Q to K/R	Q to A/C
GLU 190	E to N/Q	E to K/H	E to A/G/C		ASN 314	N to D/E	N to K/R	N to A/C
ASP 209	D to N/Q	D to K/H	D to A/G/C		GLU 345	E to N/Q	E to K/H	E to A/G/C
HIS 210	H to S/T/C	H to D/E	H to Q/N		TRP 347	W to N/Q	W to A/G/C	W to K/H
VAL 214	V to Q/N	V to G/A/C	V to K/H/D		ASP 406	D to N/Q	D to K/H	D to A/G/C
LYS 242	K to S/T/C	K to D/E	K to Q/N		HIS 407	H to S/T/C	H to D/E	H to Q/N
SER 244	S to K/R	S to Q/N/A	S to D/E/C		HIS 408	H to S/T/C	H to D/E	H to Q/N
ARG 247	R to K/H	R to Q/N	R to A/C/E		ALA 434	A to N/Q	A to K/R	A to D/E
					ASN 437	N to D/E	N to K/R	N to A/C
					ASN 475	N to D/E	N to K/R	N to A/C
					GLY 476	G to S/T	G to N/Q	G to K/D
					SER 478	S to K/R	S to Q/N/A	S to D/E/C

Example 5

Conjugation of Savinase variant R241K with activated bis-PEG-1000

228 mg of the Savinase variant was incubated in 50 mM Sodium Borate pH 9.5 with 510 mg of N-succinimidyl carbonate activated bis-PEG 1000 in a reaction volume of approximately 30 ml. The reaction was carried out at ambient temperature using magnetic stirring while keeping the pH within the interval 9.0-9.5 by addition of 0.5 M NaOH. The reaction time was 2 hours. The reaction was stopped by adding 1M HCl to a final pH of 6.0. Reagent excess was removed by ultra filtration using a Filtron-Ultrasette and the final product stored at -20°C, in 50 mM Sodium Borate, 150 mM NaCl, 1 mM CaCl2, 50% mono propylene glycol at H 6.0.
Compared to the parent enzyme, residual activity was close to 100% towards a peptide substrate (succinyl-Ala-Ala-Pro-Phe-p-nitro-anilide).

Example 6

Conjugation of Savinase variant R241K with activated bis-PEG-2000

353 mg of the Savinase variant was incubated in 50 mM Sodium Borate pH 9.5 with 1621 mg of N-succinimidyl carbonate activated bis-PEG 2000 in a reaction volume of approximately 35 ml. The reaction was carried out at ambient temperature using magnetic stirring while keeping the pH within the interval 9.0-9.5 by addition of 0.5 M NaOH. The reaction time was 2 hours. The reaction was stopped by adding 1M HCl to a final pH of 6.0. Reagent excess was removed by ultra filtration using a Filtron-Ultrasette and the final product stored at -20°C, in 50 mM Sodium Borate, 150 mM NaCl, 1 mM CaCl2, 50% mono propylene glycol at H 6.0.

Compared to the parent enzyme, residual activity was close to 100% towards a peptide substrate (succinyl-Ala-Ala-Pro-Phe-p-nitro-anilide).

Example 7

Determination of IgE levels in rats of R241KbPEG1000 and R241KbPEG2000

Methods:

Sample Management: Each sample was diluted to 0.075 mg protein/ml, and aliquoted in 1.5 ml. These fractions were sent to the stables for storage at -20°C until use. Additionally, 100 µl of the respective fractions were stored in the lab-freezer at -20°C for immunochemical analysis at the beginning, halfway and at the end of the study. For each immunization and each analysis a new fraction was taken.

Immunization: Twenty intratracheal immunizations were performed weekly with 100 µl 0.9% (wt/vol) NaCl (control group), or 100 µl of the protein dilution mentioned before. (group 5 unmodified R241K variant of Savinase, group 6 R241K-bis-S-PEG1000, and group 7 R241K-bis-S-PEG2000. Each group contained 10 rats. Blood samples (2 ml) were collected from the eye one week after every second immunization. Serum was obtained by blood clothing, and centrifugation.

ELISA: Specific IgE levels were determined using the ELISA's specific for rat IgE. The sera were titrated at ½ dilutions, starting from undiluted. Optical densities were measured at 492/620 nm.

The results are shown in figure 1. As can be seen the IgE levels of the conjugated savinase variants R241K are reduced compared to the savinase variant R241K.

Example 8

Determination of IgE levels in mice of savinase variants

R241Q, R241E, R241H and R241K.

Female Balb/c mice, 9 weeks of age were immunised subcutaneously for 20 consecutive weeks, with wild type savinase, and with variants having single mutations in position R241 (R241Q, R241E, R241H, R241K). Every other week, IgG1 and IgE serum levels were determined by ELISA.

Sample Management: Each sample was diluted to 0.010 mg protein/ml, and aliquoted in 1.5 ml. These fractions were sent to the stables for storage at -20°C until use. Additionally, 100 µl of the respective fractions were stored in the lab-freezer at -20°C for immunochemical analysis at the beginning, halfway and at the end of the study. For each immunization and each analysis a new fraction was taken.

Immunization: Twenty subcutanuous immunizations were performed weekly with 100 µl 0.9% (wt/vol) NaCl (control group), or 100 µl of the protein dilution mentioned before. Thus, group 1 received wild type Savinase, group 2 (R241Q), group 3 (R241H), group 4 (R241E), and group 5 (R241K). Each group contained 10 mice. Blood samples (100 µl) were collected from the eye one week after every second immunization. Serum was obtained by blood clotting, and centrifugation.

ELISA: Specific IgG1 levels were determined using the ELISA specific for mouse IgG1. The sera were titrated at ½ dilutions, starting from 1:160.

Specific IgE levels were determined using the ELISAs specific for mouse IgE. The sera were titrated at ½ dilutions, starting from undiluted. Optical densities were measured at 492/620 nm.

Statistical analysis: Differences between data sets were analysed by using nonparametric methods: the Kruskal-Wallis Test and the Dunn's Multiple Comparison Test.

The results are shown in figure 2. As can be seen the IgE levels of the Savinase variants are significantly reduced.

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APPENDIX 1

The structure of PD498 as determined by X-ray crystallography in Brookhaven Protein Data Bank (PDB) format.

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CRYST    45.070   67.090   81.100  90.00  90.00  90.00 P212121
SCALE1       0.02219   0.00000   0.00000         0.00000
SCALE2       0.00000   0.01491   0.00000         0.00000
SCALE3       0.00000   0.00000   0.01233         0.00000
ATOM      1  N   TRP A   1      17.560 -14.241  47.742  1.00 15.33    7
ATOM      2  CA  TRP A   1      18.953 -13.784  47.487  1.00 15.36    6
ATOM      3  C   TRP A   1      19.164 -12.349  48.002  1.00 14.46    6
ATOM      4  O   TRP A   1      18.277 -11.567  47.654  1.00 17.10    8
ATOM      5  CB  TRP A   1      19.316 -13.777  46.000  1.00 21.00    6
ATOM      6  CG  TRP A   1      20.729 -13.519  45.607  1.00 15.22    6
ATOM      7  CD1 TRP A   1      21.877 -14.241  45.845  1.00 14.54    6
ATOM      8  CD2 TRP A   1      21.184 -12.390  44.857  1.00 16.51    6
ATOM      9  NE1 TRP A   1      22.998 -13.643  45.245  1.00 18.87    7
ATOM     10  CE2 TRP A   1      22.542 -12.469  44.624  1.00 14.70    6
ATOM     11  CE3 TRP A   1      20.514 -11.271  44.272  1.00 20.67    6
ATOM     12  CZ2 TRP A   1      23.347 -11.559  43.931  1.00 20.48    6
ATOM     13  CZ3 TRP A   1      21.309 -10.381  43.596  1.00 16.65    6
ATOM     14  CH2 TRP A   1      22.661 -10.472  43.360  1.00 16.74    6
ATOM     15  N   SER A   2      20.202 -12.093  48.812  1.00 13.43    7
ATOM     16  CA  SER A   2      20.289 -10.697  49.312  1.00 15.64    6
ATOM     17  C   SER A   2      21.710 -10.249  49.014  1.00 15.52    6
ATOM     18  O   SER A   2      22.776 -10.605  49.501  1.00 18.28    8
ATOM     19  CB  SER A   2      19.980 -10.591  50.815  1.00 25.19    6
ATOM     20  OG  SER A   2      18.701 -11.130  51.119  1.00 27.27    8
ATOM     21  N   PRO A   3      21.785  -9.317  48.032  1.00 14.76    7
ATOM     22  CA  PRO A   3      23.056  -8.803  47.578  1.00 14.21    6
ATOM     23  C   PRO A   3      23.708  -7.855  48.606  1.00 14.51    6
ATOM     24  O   PRO A   3      23.048  -7.406  49.556  1.00 14.63    8
ATOM     25  CB  PRO A   3      22.743  -8.050  46.281  1.00 12.74    6
ATOM     26  CG  PRO A   3      21.293  -7.620  46.498  1.00 14.64    6
ATOM     27  CD  PRO A   3      20.663  -8.776  47.270  1.00 14.83    6
ATOM     28  N   ASN A   4      25.005  -7.718  48.445  1.00 10.92    7
ATOM     29  CA  ASN A   4      25.792  -7.034  49.477  1.00 13.99    6
ATOM     30  C   ASN A   4      25.899  -5.526  49.311  1.00 13.94    6
ATOM     31  O   ASN A   4      26.667  -4.870  50.046  1.00 12.98    8
ATOM     32  CB  ASN A   4      27.215  -7.626  49.502  1.00 12.72    6
ATOM     33  CG  ASN A   4      28.075  -7.328  48.321  1.00 16.43    6
ATOM     34  OD1 ASN A   4      27.647  -6.473  47.509  1.00 14.80    8
ATOM     35  ND2 ASN A   4      29.265  -7.911  48.155  1.00 18.33    7
ATOM     36  N   ASP A   5      25.165  -4.896  48.360  1.00 11.85    7
ATOM     37  CA  ASP A   5      25.401  -3.474  48.156  1.00 12.19    6
ATOM     38  C   ASP A   5      25.065  -2.624  49.348  1.00 11.69    6
ATOM     39  O   ASP A   5      23.954  -2.816  49.936  1.00 10.53    8
ATOM     40  CB  ASP A   5      24.570  -2.988  46.920  1.00 10.10    6
ATOM     41  CG  ASP A   5      24.777  -4.005  45.780  1.00  9.83    6
ATOM     42  OD1 ASP A   5      24.199  -5.106  45.756  1.00 12.14    8
ATOM     43  OD2 ASP A   5      25.568  -3.642  44.871  1.00 12.15    8
ATOM     44  N   PRO A   6      25.900  -1.745  49.795  1.00 11.28    7
ATOM     45  CA  PRO A   6      25.673  -1.089  51.084  1.00 11.29    6
ATOM     46  C   PRO A   6      24.481  -0.190  51.146  1.00 11.12    6
ATOM     47  O   PRO A   6      23.759  -0.196  52.180  1.00 12.14    8
ATOM     48  CB  PRO A   6      26.984  -0.356  51.426  1.00 12.53    6
ATOM     49  CG  PRO A   6      27.599  -0.217  50.014  1.00 14.20    6
ATOM     50  CD  PRO A   6      27.226  -1.453  49.202  1.00 11.88    6
ATOM     51  N   TYR A   7      24.143   0.465  50.046  1.00 11.91    7
ATOM     52  CA  TYR A   7      23.015   1.415  50.137  1.00 12.11    6
ATOM     53  C   TYR A   7      21.733   0.635  49.875  1.00 11.41    6
ATOM     54  O   TYR A   7      20.642   1.099  50.172  1.00 11.81    8
ATOM     55  CB  TYR A   7      23.237   2.509  49.078  1.00 13.43    6
ATOM     56  CG  TYR A   7      24.375   3.451  49.407  1.00 16.52    6
ATOM     57  CD1 TYR A   7      24.897   3.394  50.732  1.00 19.41    6
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	ATOM	58	CD2	TYR	A	7	24.900	4.310	48.518	1.00	25.90	6
	ATOM	59	CE1	TYR	A	7	25.932	4.231	51.078	1.00	23.70	6
	ATOM	60	CE2	TYR	A	7	25.942	5.152	48.885	1.00	25.53	6
	ATOM	61	CZ	TYR	A	7	26.454	5.099	50.157	1.00	30.83	6
5	ATOM	62	OH	TYR	A	7	27.491	5.983	50.400	1.00	33.22	8
	ATOM	63	N	TYR	A	8	21.819	-0.575	49.311	1.00	11.44	7
	ATOM	64	CA	TYR	A	8	20.685	-1.490	49.258	1.00	10.93	6
	ATOM	65	C	TYR	A	8	20.237	-1.852	50.698	1.00	10.97	6
	ATOM	66	O	TYR	A	8	19.073	-1.666	51.030	1.00	10.70	8
10	ATOM	67	CB	TYR	A	8	20.975	-2.737	48.431	1.00	11.45	6
	ATOM	68	CG	TYR	A	8	19.938	-3.813	48.547	1.00	8.84	6
	ATOM	69	CD1	TYR	A	8	18.683	-3.646	47.894	1.00	10.94	6
	ATOM	70	CD2	TYR	A	8	20.110	-4.990	49.259	1.00	10.83	6
	ATOM	71	CE1	TYR	A	8	17.705	-4.627	47.983	1.00	10.64	6
15	ATOM	72	CE2	TYR	A	8	19.112	-5.961	49.350	1.00	12.45	6
	ATOM	73	CZ	TYR	A	8	17.902	-5.782	48.678	1.00	12.68	6
	ATOM	74	OH	TYR	A	8	16.908	-6.733	48.789	1.00	13.25	8
	ATOM	75	N	SER	A	9	21.247	-2.270	51.460	1.00	10.94	7
	ATOM	76	CA	SER	A	9	20.949	-2.660	52.854	1.00	11.34	6
20	ATOM	77	C	SER	A	9	20.483	-1.450	53.656	1.00	9.76	6
	ATOM	78	O	SER	A	9	19.549	-1.582	54.465	1.00	11.69	8
	ATOM	79	CB	SER	A	9	22.271	-3.179	53.448	1.00	12.98	6
	ATOM	80	OG	SER	A	9	21.986	-3.491	54.840	1.00	14.32	8
	ATOM	81	N	ALA	A	10	21.018	-0.283	53.428	1.00	9.72	7
25	ATOM	82	CA	ALA	A	10	20.805	0.860	54.332	1.00	9.30	6
	ATOM	83	C	ALA	A	10	19.596	1.655	53.965	1.00	12.42	6
	ATOM	84	O	ALA	A	10	18.883	2.230	54.794	1.00	11.71	8
	ATOM	85	CB	ALA	A	10	22.036	1.757	54.363	1.00	12.70	6
	ATOM	86	N	TYR	A	11	19.352	1.779	52.621	1.00	12.14	7
30	ATOM	87	CA	TYR	A	11	18.374	2.754	52.188	1.00	11.21	6
	ATOM	88	C	TYR	A	11	17.339	2.269	51.177	1.00	12.10	6
	ATOM	89	O	TYR	A	11	16.323	2.972	51.018	1.00	11.98	8
	ATOM	90	CB	TYR	A	11	19.141	3.914	51.448	1.00	9.82	6
	ATOM	91	CG	TYR	A	11	20.208	4.587	52.293	1.00	11.77	6
35	ATOM	92	CD1	TYR	A	11	19.815	5.317	53.419	1.00	15.20	6
	ATOM	93	CD2	TYR	A	11	21.541	4.493	51.970	1.00	16.78	6
	ATOM	94	CE1	TYR	A	11	20.773	5.955	54.196	1.00	17.43	6
	ATOM	95	CE2	TYR	A	11	22.494	5.125	52.756	1.00	19.92	6
	ATOM	96	CZ	TYR	A	11	22.084	5.837	53.864	1.00	18.68	6
40	ATOM	97	OH	TYR	A	11	23.095	6.450	54.626	1.00	20.61	8
	ATOM	98	N	GLN	A	12	17.490	1.075	50.573	1.00	9.57	7
	ATOM	99	CA	GLN	A	12	16.421	0.747	49.622	1.00	10.23	6
	ATOM	100	C	GLN	A	12	15.251	0.052	50.260	1.00	9.88	6
	ATOM	101	O	GLN	A	12	15.422	-0.710	51.235	1.00	10.94	8
45	ATOM	102	CB	GLN	A	12	16.984	-0.155	48.471	1.00	10.30	6
	ATOM	103	CG	GLN	A	12	17.846	0.612	47.491	1.00	9.41	6
	ATOM	104	CD	GLN	A	12	18.378	-0.293	46.387	1.00	9.03	6
	ATOM	105	OE1	GLN	A	12	19.616	-0.526	46.434	1.00	10.69	8
	ATOM	106	NE2	GLN	A	12	17.572	-0.688	45.438	1.00	9.50	7
50	ATOM	107	N	TYR	A	13	14.053	0.139	49.639	1.00	8.12	7
	ATOM	108	CA	TYR	A	13	12.931	-0.656	50.006	1.00	8.04	6
	ATOM	109	C	TYR	A	13	12.175	-1.201	48.793	1.00	11.46	6
	ATOM	110	O	TYR	A	13	11.392	-2.128	48.912	1.00	10.57	8
	ATOM	111	CB	TYR	A	13	11.899	0.042	50.915	1.00	8.33	6
55	ATOM	112	CG	TYR	A	13	11.153	1.131	50.181	1.00	8.81	6
	ATOM	113	CD1	TYR	A	13	9.906	0.863	49.604	1.00	8.32	6
	ATOM	114	CD2	TYR	A	13	11.653	2.441	50.097	1.00	8.79	6
	ATOM	115	CE1	TYR	A	13	9.192	1.837	48.913	1.00	9.23	6
	ATOM	116	CE2	TYR	A	13	10.942	3.429	49.381	1.00	7.86	6
60	ATOM	117	CZ	TYR	A	13	9.687	3.114	48.835	1.00	9.91	6
	ATOM	118	OH	TYR	A	13	8.956	4.116	48.210	1.00	10.94	8
	ATOM	119	N	GLY	A	14	12.538	-0.722	47.591	1.00	10.19	7
	ATOM	120	CA	GLY	A	14	11.702	-1.114	46.428	1.00	10.55	6
	ATOM	121	C	GLY	A	14	11.732	-2.616	46.134	1.00	11.11	6
65	ATOM	122	O	GLY	A	14	10.681	-3.246	45.967	1.00	11.34	8
	ATOM	123	N	PRO	A	15	12.909	-3.176	46.030	1.00	8.71	7
	ATOM	124	CA	PRO	A	15	12.958	-4.630	45.810	1.00	9.03	6
	ATOM	125	C	PRO	A	15	12.372	-5.426	46.996	1.00	10.83	6

	ATOM	126	O	PRO	A	15	11.557	-6.333	46.772	1.00	10.41	8
	ATOM	127	CB	PRO	A	15	14.480	-4.906	45.683	1.00	10.96	6
	ATOM	128	CG	PRO	A	15	15.102	-3.549	45.304	1.00	9.61	6
	ATOM	129	CD	PRO	A	15	14.229	-2.508	46.030	1.00	9.57	6
5	ATOM	130	N	GLN	A	16	12.741	-5.038	48.222	1.00	10.84	7
	ATOM	131	CA	GLN	A	16	12.216	-5.795	49.382	1.00	9.58	6
	ATOM	132	C	GLN	A	16	10.677	-5.822	49.420	1.00	9.41	6
	ATOM	133	O	GLN	A	16	10.047	-6.896	49.711	1.00	12.05	8
	ATOM	134	CB	GLN	A	16	12.784	-5.110	50.653	1.00	9.56	6
10	ATOM	135	CG	GLN	A	16	14.295	-5.237	50.750	1.00	10.85	6
	ATOM	136	CD	GLN	A	16	15.079	-4.045	50.301	1.00	9.18	6
	ATOM	137	OE1	GLN	A	16	14.615	-3.357	49.328	1.00	11.39	8
	ATOM	138	NE2	GLN	A	16	16.242	-3.776	50.867	1.00	10.81	7
	ATOM	139	N	ASN	A	17	10.073	-4.629	49.215	1.00	10.52	7
15	ATOM	140	CA	ASN	A	17	8.627	-4.532	49.347	1.00	9.85	6
	ATOM	141	C	ASN	A	17	7.909	-5.151	48.185	1.00	11.20	6
	ATOM	142	O	ASN	A	17	6.658	-5.131	48.244	1.00	14.71	8
	ATOM	143	CB	ASN	A	17	8.208	-3.046	49.509	1.00	11.59	6
	ATOM	144	CG	ASN	A	17	8.432	-2.520	50.937	1.00	13.87	6
20	ATOM	145	OD1	ASN	A	17	9.226	-3.101	51.658	1.00	13.47	8
	ATOM	146	ND2	ASN	A	17	7.687	-1.460	51.259	1.00	12.64	7
	ATOM	147	N	THR	A	18	8.566	-5.563	47.128	1.00	10.29	7
	ATOM	148	CA	THR	A	18	7.890	-6.216	45.992	1.00	12.51	6
	ATOM	149	C	THR	A	18	8.300	-7.680	45.974	1.00	12.13	6
25	ATOM	150	O	THR	A	18	8.100	-8.386	44.963	1.00	11.44	8
	ATOM	151	CB	THR	A	18	8.244	-5.529	44.659	1.00	9.68	6
	ATOM	152	OG1	THR	A	18	9.696	-5.431	44.525	1.00	10.42	8
	ATOM	153	CG2	THR	A	18	7.591	-4.187	44.624	1.00	12.66	6
	ATOM	154	N	SER	A	19	8.884	-8.204	47.078	1.00	10.54	7
30	ATOM	155	CA	SER	A	19	9.287	-9.606	47.140	1.00	12.19	6
	ATOM	156	C	SER	A	19	10.334	-9.982	46.079	1.00	10.66	6
	ATOM	157	O	SER	A	19	10.372	-11.143	45.609	1.00	11.55	8
	ATOM	158	CB	SER	A	19	8.113	-10.594	47.058	1.00	15.77	6
	ATOM	159	OG	SER	A	19	7.242	-10.315	48.179	1.00	14.40	8
35	ATOM	160	N	THR	A	20	11.176	-9.000	45.757	1.00	11.05	7
	ATOM	161	CA	THR	A	20	12.179	-9.303	44.731	1.00	9.03	6
	ATOM	162	C	THR	A	20	13.341	-10.159	45.212	1.00	10.84	6
	ATOM	163	O	THR	A	20	13.841	-10.974	44.462	1.00	12.64	8
	ATOM	164	CB	THR	A	20	12.652	-8.005	44.067	1.00	11.34	6
40	ATOM	165	OG1	THR	A	20	11.486	-7.307	43.584	1.00	10.88	8
	ATOM	166	CG2	THR	A	20	13.563	-8.230	42.867	1.00	13.97	6
	ATOM	167	N	PRO	A	21	13.788	-10.140	46.474	1.00	10.13	7
	ATOM	168	CA	PRO	A	21	14.814	-11.028	46.940	1.00	10.60	6
	ATOM	169	C	PRO	A	21	14.417	-12.506	46.749	1.00	11.26	6
45	ATOM	170	O	PRO	A	21	15.311	-13.256	46.270	1.00	13.61	8
	ATOM	171	CB	PRO	A	21	14.916	-10.701	48.467	1.00	10.30	6
	ATOM	172	CG	PRO	A	21	14.710	-9.205	48.354	1.00	10.51	6
	ATOM	173	CD	PRO	A	21	13.477	-9.064	47.464	1.00	10.93	6
	ATOM	174	N	ALA	A	22	13.151	-12.862	46.938	1.00	12.78	7
50	ATOM	175	CA	ALA	A	22	12.706	-14.246	46.639	1.00	13.32	6
	ATOM	176	C	ALA	A	22	12.644	-14.482	45.123	1.00	14.57	6
	ATOM	177	O	ALA	A	22	13.070	-15.576	44.679	1.00	15.26	8
	ATOM	178	CB	ALA	A	22	11.317	-14.454	47.282	1.00	13.94	6
	ATOM	179	N	ALA	A	23	12.273	-13.425	44.396	1.00	12.81	7
55	ATOM	180	CA	ALA	A	23	12.317	-13.614	42.917	1.00	14.03	6
	ATOM	181	C	ALA	A	23	13.716	-13.880	42.477	1.00	12.10	6
	ATOM	182	O	ALA	A	23	13.915	-14.577	41.425	1.00	12.81	8
	ATOM	183	CB	ALA	A	23	11.712	-12.341	42.261	1.00	12.05	6
	ATOM	184	N	TRP	A	24	14.752	-13.217	42.989	1.00	11.24	7
60	ATOM	185	CA	TRP	A	24	16.128	-13.387	42.591	1.00	11.78	6
	ATOM	186	C	TRP	A	24	16.654	-14.840	42.845	1.00	13.08	6
	ATOM	187	O	TRP	A	24	17.723	-15.104	42.305	1.00	15.03	8
	ATOM	188	CB	TRP	A	24	16.971	-12.366	43.334	1.00	15.91	6
	ATOM	189	CG	TRP	A	24	16.890	-10.942	42.898	1.00	12.46	6
65	ATOM	190	CD1	TRP	A	24	16.549	-10.488	41.656	1.00	11.81	6
	ATOM	191	CD2	TRP	A	24	17.146	-9.775	43.673	1.00	12.89	6
	ATOM	192	NE1	TRP	A	24	16.584	-9.109	41.590	1.00	11.12	7
	ATOM	193	CE2	TRP	A	24	16.965	-8.633	42.853	1.00	11.48	6

ATOM	194	CE3	TRP	A	24	17.514	-9.554	45.015	1.00	14.60	6
ATOM	195	CZ2	TRP	A	24	17.132	-7.300	43.254	1.00	12.39	6
ATOM	196	CZ3	TRP	A	24	17.643	-8.268	45.452	1.00	12.43	6
ATOM	197	CH2	TRP	A	24	17.501	-7.164	44.601	1.00	11.45	6
ATOM	198	N	ASP	A	25	15.955	-15.602	43.660	1.00	16.22	7
ATOM	199	CA	ASP	A	25	16.307	-17.019	43.816	1.00	19.28	6
ATOM	200	C	ASP	A	25	16.013	-17.758	42.511	1.00	19.51	6
ATOM	201	O	ASP	A	25	16.674	-18.766	42.232	1.00	21.06	8
ATOM	202	CB	ASP	A	25	15.474	-17.590	44.987	1.00	15.40	6
ATOM	203	CG	ASP	A	25	15.889	-17.050	46.378	1.00	16.84	6
ATOM	204	OD1	ASP	A	25	14.914	-16.931	47.182	1.00	20.99	8
ATOM	205	OD2	ASP	A	25	17.069	-16.798	46.451	1.00	18.83	8
ATOM	206	N	VAL	A	26	15.083	-17.234	41.717	1.00	16.85	7
ATOM	207	CA	VAL	A	26	14.677	-17.883	40.450	1.00	16.29	6
ATOM	208	C	VAL	A	26	15.490	-17.307	39.300	1.00	14.78	6
ATOM	209	O	VAL	A	26	16.049	-18.044	38.463	1.00	16.30	8
ATOM	210	CB	VAL	A	26	13.181	-17.689	40.253	1.00	15.77	6
ATOM	211	CG1	VAL	A	26	12.727	-18.260	38.878	1.00	16.26	6
ATOM	212	CG2	VAL	A	26	12.288	-18.249	41.341	1.00	14.73	6
ATOM	213	N	THR	A	27	15.627	-15.970	39.244	1.00	13.62	7
ATOM	214	CA	THR	A	27	16.434	-15.392	38.191	1.00	13.55	6
ATOM	215	C	THR	A	27	16.969	-13.994	38.562	1.00	13.11	6
ATOM	216	O	THR	A	27	16.239	-13.327	39.294	1.00	12.83	8
ATOM	217	CB	THR	A	27	15.570	-15.267	36.899	1.00	16.42	6
ATOM	218	OG1	THR	A	27	16.481	-14.652	35.997	1.00	20.55	8
ATOM	219	CG2	THR	A	27	14.260	-14.538	37.127	1.00	15.35	6
ATOM	220	N	ARG	A	28	18.167	-13.715	38.082	1.00	13.95	7
ATOM	221	CA	ARG	A	28	18.707	-12.376	38.350	1.00	14.11	6
ATOM	222	C	ARG	A	28	18.914	-11.569	37.058	1.00	13.63	6
ATOM	223	O	ARG	A	28	19.518	-10.522	37.077	1.00	13.70	8
ATOM	224	CB	ARG	A	28	20.007	-12.487	39.167	1.00	13.10	6
ATOM	225	CG	AARG	A	28	19.786	-12.592	40.676	0.50	16.44	6
ATOM	226	CD	AARG	A	28	21.015	-13.229	41.319	0.50	13.92	6
ATOM	227	NE	AARG	A	28	21.173	-14.653	40.989	0.50	20.11	7
ATOM	228	CZ	AARG	A	28	22.394	-15.198	41.007	0.50	22.04	6
ATOM	229	NH1	AARG	A	28	23.372	-14.370	41.347	0.50	16.08	7
ATOM	230	NH2	AARG	A	28	22.629	-16.456	40.719	0.50	19.93	7
ATOM	231	CG	BARG	A	28	19.609	-13.094	40.526	0.50	12.85	6
ATOM	232	CD	BARG	A	28	20.809	-13.394	41.414	0.50	12.14	6
ATOM	233	NE	BARG	A	28	21.589	-14.471	40.795	0.50	12.31	7
ATOM	234	CZ	BARG	A	28	21.281	-15.746	40.991	0.50	10.72	6
ATOM	235	NH1	BARG	A	28	20.289	-16.183	41.754	0.50	13.92	7
ATOM	236	NH2	BARG	A	28	22.032	-16.678	40.382	0.50	18.15	7
ATOM	237	N	GLY	A	29	18.305	-12.018	35.941	1.00	12.92	7
ATOM	238	CA	GLY	A	29	18.362	-11.296	34.672	1.00	12.43	6
ATOM	239	C	GLY	A	29	19.326	-12.019	33.736	1.00	11.85	6
ATOM	240	O	GLY	A	29	19.589	-13.202	33.991	1.00	16.10	8
ATOM	241	N	SER	A	330	19.705	-11.325	32.693	1.00	11.08	7
ATOM	242	CA	SER	A	330	20.543	-11.993	31.666	1.00	12.22	6
ATOM	243	C	SER	A	330	21.461	-10.943	31.078	1.00	13.35	6
ATOM	244	O	SER	A	330	21.121	-9.889	30.574	1.00	13.86	8
ATOM	245	CB	SER	A	330	19.712	-12.583	30.525	1.00	15.19	6
ATOM	246	OG	SER	A	330	20.650	-12.917	29.463	1.00	17.47	8
ATOM	247	N	SER	A	331	22.855	-11.292	31.059	1.00	14.23	7
ATOM	248	CA	SER	A	331	23.828	-10.406	30.487	1.00	13.69	6
ATOM	249	C	SER	A	331	23.784	-10.224	28.959	1.00	12.34	6
ATOM	250	O	SER	A	331	24.497	-9.322	28.490	1.00	19.86	8
ATOM	251	CB	SER	A	331	25.268	-10.725	30.898	1.00	18.58	6
ATOM	252	OG	SER	A	331	25.541	-12.037	30.388	1.00	22.11	8
ATOM	253	N	THR	A	332	22.962	-11.067	28.421	1.00	11.83	7
ATOM	254	CA	THR	A	332	22.892	-10.969	26.958	1.00	15.40	6
ATOM	255	C	THR	A	332	21.538	-10.413	26.518	1.00	17.11	6
ATOM	256	O	THR	A	332	21.235	-10.376	25.323	1.00	16.83	8
ATOM	257	CB	THR	A	332	22.969	-12.367	26.285	1.00	17.26	6
ATOM	258	OG1	THR	A	332	22.107	-13.305	26.854	1.00	22.90	8
ATOM	259	CG2	THR	A	332	24.448	-12.815	26.411	1.00	22.90	6
ATOM	260	N	GLN	A	333	20.861	-9.716	27.512	1.00	13.07	7
ATOM	261	CA	GLN	A	333	19.630	-8.974	27.160	1.00	12.63	6

ATOM	262	C	GLN	A	333	19.830	-7.523	27.631	1.00	13.44	6
ATOM	263	O	GLN	A	333	20.686	-7.227	28.461	1.00	12.88	8
ATOM	264	CB	GLN	A	333	18.420	-9.526	27.862	1.00	10.82	6
ATOM	265	CG	GLN	A	333	18.173	-10.962	27.360	1.00	12.25	6
ATOM	266	CD	GLN	A	333	16.999	-11.643	27.966	1.00	11.24	6
ATOM	267	OE1	GLN	A	333	16.554	-11.300	29.074	1.00	13.22	8
ATOM	268	NE2	GLN	A	333	16.375	-12.657	27.326	1.00	16.24	7
ATOM	269	N	THR	A	33	18.960	-6.642	27.102	1.00	11.79	7
ATOM	270	CA	THR	A	33	18.984	-5.248	27.523	1.00	11.06	6
ATOM	271	C	THR	A	33	17.582	-4.748	27.909	1.00	12.71	6
ATOM	272	O	THR	A	33	16.558	-5.185	27.394	1.00	10.99	8
ATOM	273	CB	THR	A	33	19.560	-4.307	26.452	1.00	12.32	6
ATOM	274	OG1	THR	A	33	18.727	-4.350	25.274	1.00	15.31	8
ATOM	275	CG2	THR	A	33	20.994	-4.701	26.098	1.00	15.29	6
ATOM	276	N	VAL	A	34	17.606	-3.738	28.781	1.00	9.33	7
ATOM	277	CA	VAL	A	34	16.448	-2.906	29.047	1.00	9.03	6
ATOM	278	C	VAL	A	34	16.817	-1.513	28.545	1.00	10.82	6
ATOM	279	O	VAL	A	34	17.894	-1.011	28.947	1.00	11.09	8
ATOM	280	CB	VAL	A	34	16.075	-2.760	30.525	1.00	11.19	6
ATOM	281	CG1	VAL	A	34	14.975	-1.712	30.731	1.00	12.05	6
ATOM	282	CG2	VAL	A	34	15.715	-4.091	31.092	1.00	14.97	6
ATOM	283	N	ALA	A	35	16.062	-0.937	27.616	1.00	9.42	7
ATOM	284	CA	ALA	A	35	16.349	0.401	27.149	1.00	12.14	6
ATOM	285	C	ALA	A	35	15.788	1.446	28.086	1.00	9.96	6
ATOM	286	O	ALA	A	35	14.616	1.449	28.408	1.00	11.17	8
ATOM	287	CB	ALA	A	35	15.810	0.631	25.724	1.00	11.54	6
ATOM	288	N	VAL	A	36	16.662	2.296	28.554	1.00	8.03	7
ATOM	289	CA	VAL	A	36	16.307	3.428	29.435	1.00	9.34	6
ATOM	290	C	VAL	A	36	16.255	4.660	28.537	1.00	9.42	6
ATOM	291	O	VAL	A	36	17.290	5.187	28.168	1.00	10.30	8
ATOM	292	CB	VAL	A	36	17.253	3.591	30.610	1.00	7.40	6
ATOM	293	CG1	VAL	A	36	16.943	4.884	31.357	1.00	12.02	6
ATOM	294	CG2	VAL	A	36	17.063	2.359	31.521	1.00	9.73	6
ATOM	295	N	LEU	A	37	15.003	4.992	28.181	1.00	8.33	7
ATOM	296	CA	LEU	A	37	14.774	6.125	27.245	1.00	9.07	6
ATOM	297	C	LEU	A	37	14.527	7.355	28.100	1.00	9.81	6
ATOM	298	O	LEU	A	37	13.443	7.499	28.695	1.00	10.06	8
ATOM	299	CB	LEU	A	37	13.552	5.776	26.380	1.00	10.14	6
ATOM	300	CG	LEU	A	37	13.933	4.661	25.362	1.00	11.82	6
ATOM	301	CD1	LEU	A	37	12.792	3.693	25.283	1.00	16.87	6
ATOM	302	CD2	LEU	A	37	14.217	5.400	24.043	1.00	15.43	6
ATOM	303	N	ASP	A	38	15.548	8.192	28.216	1.00	9.99	7
ATOM	304	CA	ASP	A	38	15.523	9.245	29.265	1.00	7.85	6
ATOM	305	C	ASP	A	38	16.535	10.334	29.014	1.00	10.38	6
ATOM	306	O	ASP	A	38	16.838	10.581	27.810	1.00	10.43	8
ATOM	307	CB	ASP	A	38	15.714	8.495	30.588	1.00	10.08	6
ATOM	308	CG	ASP	A	38	15.095	9.159	31.806	1.00	9.45	6
ATOM	309	OD1	ASP	A	38	15.411	10.307	32.115	1.00	11.41	8
ATOM	310	OD2	ASP	A	38	14.232	8.509	32.424	1.00	11.17	8
ATOM	311	N	SER	A	39	17.006	11.024	30.039	1.00	8.46	7
ATOM	312	CA	SER	A	39	17.914	12.155	29.835	1.00	9.33	6
ATOM	313	C	SER	A	39	19.333	11.738	29.583	1.00	10.03	6
ATOM	314	O	SER	A	39	20.239	12.604	29.544	1.00	12.39	8
ATOM	315	CB	SER	A	39	17.825	13.046	31.076	1.00	10.11	6
ATOM	316	OG	SER	A	39	18.301	12.377	32.234	1.00	11.06	8
ATOM	317	N	GLY	A	40	19.611	10.436	29.422	1.00	10.54	7
ATOM	318	CA	GLY	A	40	20.956	9.937	29.276	1.00	11.06	6
ATOM	319	C	GLY	A	40	21.309	9.106	30.504	1.00	11.64	6
ATOM	320	O	GLY	A	40	20.508	9.044	31.415	1.00	12.31	8
ATOM	321	N	VAL	A	41	22.464	8.494	30.478	1.00	11.73	7
ATOM	322	CA	VAL	A	41	22.862	7.692	31.677	1.00	10.62	6
ATOM	323	C	VAL	A	41	24.328	8.026	31.875	1.00	11.66	6
ATOM	324	O	VAL	A	41	25.086	7.934	30.912	1.00	13.26	8
ATOM	325	CB	VAL	A	41	22.679	6.202	31.427	1.00	10.61	6
ATOM	326	CG1	VAL	A	41	23.194	5.368	32.618	1.00	10.20	6
ATOM	327	CG2	VAL	A	41	21.181	5.897	31.236	1.00	11.88	6
ATOM	328	N	ASP	A	42	24.763	8.180	33.136	1.00	11.44	7
ATOM	329	CA	ASP	A	42	26.196	8.426	33.402	1.00	13.13	6

ATOM	330	C	ASP	A	42	26.852	7.060	33.461	1.00	12.56	6
ATOM	331	O	ASP	A	42	26.966	6.459	34.518	1.00	13.21	8
ATOM	332	CB	ASP	A	42	26.379	9.170	34.745	1.00	13.74	6
ATOM	333	CG	ASP	A	42	27.857	9.433	35.018	1.00	18.39	6
ATOM	334	OD1	ASP	A	42	28.140	10.034	36.082	1.00	21.20	8
ATOM	335	OD2	ASP	A	42	28.672	9.005	34.208	1.00	12.32	8
ATOM	336	N	TYR	A	43	27.358	6.645	32.283	1.00	11.92	7
ATOM	337	CA	TYR	A	43	27.980	5.350	32.095	1.00	12.00	6
ATOM	338	C	TYR	A	43	29.429	5.271	32.714	1.00	13.62	6
ATOM	339	O	TYR	A	43	29.966	4.179	32.656	1.00	14.17	8
ATOM	340	CB	TYR	A	43	28.031	4.952	30.604	1.00	14.19	6
ATOM	341	CG	TYR	A	43	28.532	6.090	29.719	1.00	13.96	6
ATOM	342	CD1	TYR	A	43	29.876	6.376	29.758	1.00	21.10	6
ATOM	343	CD2	TYR	A	43	27.649	6.817	28.949	1.00	13.89	6
ATOM	344	CE1	TYR	A	43	30.377	7.422	28.982	1.00	23.78	6
ATOM	345	CE2	TYR	A	43	28.162	7.877	28.152	1.00	17.35	6
ATOM	346	CZ	TYR	A	43	29.499	8.136	28.197	1.00	21.91	6
ATOM	347	OH	TYR	A	43	30.054	9.174	27.458	1.00	25.51	8
ATOM	348	N	ASN	A	44	29.860	6.400	33.220	1.00	14.70	7
ATOM	349	CA	ASN	A	44	31.144	6.357	33.963	1.00	15.55	6
ATOM	350	C	ASN	A	44	30.923	6.074	35.433	1.00	14.58	6
ATOM	351	O	ASN	A	44	31.889	5.965	36.221	1.00	14.97	8
ATOM	352	CB	ASN	A	44	31.874	7.711	33.833	1.00	15.61	6
ATOM	353	CG	ASN	A	44	32.294	7.939	32.344	1.00	13.41	6
ATOM	354	OD1	ASN	A	44	32.052	9.147	32.103	1.00	22.06	8
ATOM	355	ND2	ASN	A	44	32.766	6.911	31.724	1.00	16.45	7
ATOM	356	N	HIS	A	45	29.653	6.081	35.908	1.00	13.02	7
ATOM	357	CA	HIS	A	45	29.474	5.865	37.376	1.00	11.13	6
ATOM	358	C	HIS	A	45	29.917	4.462	37.727	1.00	10.90	6
ATOM	359	O	HIS	A	45	29.653	3.499	37.064	1.00	11.84	8
ATOM	360	CB	HIS	A	45	27.929	5.959	37.618	1.00	13.07	6
ATOM	361	CG	HIS	A	45	27.519	6.069	39.068	1.00	11.25	6
ATOM	362	ND1	HIS	A	45	27.779	5.071	40.007	1.00	11.49	7
ATOM	363	CD2	HIS	A	45	26.921	7.129	39.661	1.00	10.98	6
ATOM	364	CE1	HIS	A	45	27.307	5.517	41.159	1.00	12.50	6
ATOM	365	NE2	HIS	A	45	26.810	6.732	41.035	1.00	11.54	7
ATOM	366	N	PRO	A	46	30.635	4.274	38.874	1.00	11.14	7
ATOM	367	CA	PRO	A	46	31.062	2.985	39.335	1.00	11.47	6
ATOM	368	C	PRO	A	46	29.978	1.921	39.380	1.00	10.59	6
ATOM	369	O	PRO	A	46	30.196	0.767	39.040	1.00	11.62	8
ATOM	370	CB	PRO	A	46	31.677	3.220	40.742	1.00	10.94	6
ATOM	371	CG	PRO	A	46	32.043	4.671	40.670	1.00	14.48	6
ATOM	372	CD	PRO	A	46	31.085	5.353	39.688	1.00	11.69	6
ATOM	373	N	ASP	A	47	28.728	2.326	39.705	1.00	12.70	7
ATOM	374	CA	ASP	A	47	27.682	1.314	39.825	1.00	11.42	6
ATOM	375	C	ASP	A	47	26.899	1.133	38.520	1.00	12.51	6
ATOM	376	O	ASP	A	47	25.902	0.416	38.521	1.00	11.59	8
ATOM	377	CB	ASP	A	47	26.702	1.688	40.990	1.00	12.16	6
ATOM	378	CG	ASP	A	47	26.587	0.469	41.896	1.00	9.76	6
ATOM	379	OD1	ASP	A	47	27.288	-0.541	41.945	1.00	10.00	8
ATOM	380	OD2	ASP	A	47	25.518	0.471	42.653	1.00	10.91	8
ATOM	381	N	LEU	A	48	27.369	1.772	37.435	1.00	10.44	7
ATOM	382	CA	LEU	A	48	26.697	1.562	36.155	1.00	11.43	6
ATOM	383	C	LEU	A	48	27.672	1.221	35.027	1.00	12.97	6
ATOM	384	O	LEU	A	48	27.191	0.683	34.023	1.00	11.53	8
ATOM	385	CB	LEU	A	48	25.972	2.837	35.638	1.00	11.21	6
ATOM	386	CG	LEU	A	48	24.787	3.235	36.572	1.00	10.61	6
ATOM	387	CD1	LEU	A	48	24.254	4.643	36.324	1.00	11.90	6
ATOM	388	CD2	LEU	A	48	23.677	2.180	36.462	1.00	13.84	6
ATOM	389	N	ALA	A	49	28.975	1.461	35.252	1.00	12.23	7
ATOM	390	CA	ALA	A	49	29.841	1.298	34.073	1.00	9.36	6
ATOM	391	C	ALA	A	49	29.855	-0.091	33.513	1.00	10.78	6
ATOM	392	O	ALA	A	49	30.048	-0.245	32.236	1.00	16.98	8
ATOM	393	CB	ALA	A	49	31.268	1.712	34.531	1.00	12.23	6
ATOM	394	N	ARG	A	50	29.747	-1.164	34.276	1.00	11.88	7
ATOM	395	CA	ARG	A	50	29.780	-2.522	33.800	1.00	11.57	6
ATOM	396	C	ARG	A	50	28.444	-2.946	33.165	1.00	12.53	6
ATOM	397	O	ARG	A	50	28.348	-4.048	32.602	1.00	16.06	8

ATOM	398	CB	ARG	A	50	30.103	-3.524	34.930	1.00	15.47	6
ATOM	399	CG	ARG	A	50	31.531	-3.240	35.482	1.00	11.83	6
ATOM	400	CD	ARG	A	50	32.055	-4.513	36.187	1.00	15.45	6
ATOM	401	NE	ARG	A	50	31.187	-4.897	37.307	1.00	16.23	7
ATOM	402	CZ	ARG	A	50	31.384	-5.965	38.064	1.00	19.96	6
ATOM	403	NH1	ARG	A	50	32.429	-6.782	37.837	1.00	22.22	7
ATOM	404	NH2	ARG	A	50	30.526	-6.230	39.057	1.00	18.50	7
ATOM	405	N	LYS	A	51	27.436	-2.075	33.346	1.00	11.50	7
ATOM	406	CA	LYS	A	51	26.104	-2.471	32.907	1.00	11.63	6
ATOM	407	C	LYS	A	51	25.570	-1.744	31.675	1.00	12.77	6
ATOM	408	O	LYS	A	51	24.582	-2.212	31.104	1.00	13.77	8
ATOM	409	CB	LYS	A	51	25.152	-2.127	34.077	1.00	12.63	6
ATOM	410	CG	LYS	A	51	25.387	-2.922	35.380	1.00	13.22	6
ATOM	411	CD	LYS	A	51	25.538	-4.413	35.201	1.00	14.71	6
ATOM	412	CE	LYS	A	51	24.312	-5.051	34.628	1.00	13.09	6
ATOM	413	NZ	LYS	A	51	23.056	-4.815	35.491	1.00	12.18	7
ATOM	414	N	VAL	A	52	26.124	-0.623	31.345	1.00	11.71	7
ATOM	415	CA	VAL	A	52	25.551	0.247	30.312	1.00	10.53	6
ATOM	416	C	VAL	A	52	26.166	0.046	28.941	1.00	14.73	6
ATOM	417	O	VAL	A	52	27.383	0.061	28.778	1.00	16.03	8
ATOM	418	CB	VAL	A	52	25.711	1.692	30.750	1.00	10.80	6
ATOM	419	CG1	VAL	A	52	25.233	2.601	29.613	1.00	15.73	6
ATOM	420	CG2	VAL	A	52	24.874	1.987	32.005	1.00	11.42	6
ATOM	421	N	ILE	A	53	25.247	-0.130	27.987	1.00	11.33	7
ATOM	422	CA	ILE	A	53	25.609	-0.098	26.552	1.00	11.76	6
ATOM	423	C	ILE	A	53	25.210	1.272	26.028	1.00	14.46	6
ATOM	424	O	ILE	A	53	24.071	1.711	26.289	1.00	13.75	8
ATOM	425	CB	ILE	A	53	24.877	-1.179	25.791	1.00	12.46	6
ATOM	426	CG1	ILE	A	53	25.331	-2.530	26.296	1.00	14.67	6
ATOM	427	CG2	ILE	A	53	25.229	-1.050	24.291	1.00	11.24	6
ATOM	428	CD1	ILE	A	53	24.535	-3.702	25.780	1.00	20.94	6
ATOM	429	N	LYS	A	54	26.112	1.975	25.367	1.00	14.25	7
ATOM	430	CA	LYS	A	54	25.812	3.317	24.896	1.00	12.81	6
ATOM	431	C	LYS	A	54	24.994	3.315	23.618	1.00	12.98	6
ATOM	432	O	LYS	A	54	25.458	2.835	22.572	1.00	17.68	8
ATOM	433	CB	LYS	A	54	27.109	4.126	24.613	1.00	13.38	6
ATOM	434	CG	LYS	A	54	27.905	4.467	25.886	1.00	13.70	6
ATOM	435	CD	LYS	A	54	29.303	4.949	25.440	1.00	23.57	6
ATOM	436	CE	LYS	A	54	30.311	4.482	26.488	1.00	25.44	6
ATOM	437	NZ	LYS	A	54	30.879	3.152	26.128	1.00	39.20	7
ATOM	438	N	GLY	A	55	23.737	3.675	23.690	1.00	12.13	7
ATOM	439	CA	GLY	A	55	22.853	3.848	22.554	1.00	12.94	6
ATOM	440	C	GLY	A	55	22.968	5.304	22.070	1.00	12.91	6
ATOM	441	O	GLY	A	55	23.771	6.146	22.479	1.00	13.22	8
ATOM	442	N	TYR	A	56	22.084	5.613	21.090	1.00	13.51	7
ATOM	443	CA	TYR	A	56	22.092	6.918	20.449	1.00	12.80	6
ATOM	444	C	TYR	A	56	21.594	8.052	21.346	1.00	14.95	6
ATOM	445	O	TYR	A	56	20.699	7.845	22.158	1.00	14.71	8
ATOM	446	CB	TYR	A	56	21.369	6.789	19.085	1.00	12.24	6
ATOM	447	CG	TYR	A	56	21.659	7.944	18.131	1.00	12.40	6
ATOM	448	CD1	TYR	A	56	22.915	7.978	17.542	1.00	15.33	6
ATOM	449	CD2	TYR	A	56	20.766	8.959	17.915	1.00	13.06	6
ATOM	450	CE1	TYR	A	56	23.255	9.010	16.664	1.00	15.12	6
ATOM	451	CE2	TYR	A	56	21.106	10.017	17.016	1.00	15.08	6
ATOM	452	CZ	TYR	A	56	22.347	10.002	16.421	1.00	16.78	6
ATOM	453	OH	TYR	A	56	22.603	11.097	15.574	1.00	20.74	8
ATOM	454	N	ASP	A	57	22.042	9.257	21.061	1.00	12.59	7
ATOM	455	CA	ASP	A	57	21.604	10.456	21.735	1.00	11.21	6
ATOM	456	C	ASP	A	57	20.882	11.313	20.683	1.00	14.11	6
ATOM	457	O	ASP	A	57	21.559	11.878	19.812	1.00	14.49	8
ATOM	458	CB	ASP	A	57	22.814	11.201	22.293	1.00	15.01	6
ATOM	459	CG	ASP	A	57	22.480	12.521	22.943	1.00	13.70	6
ATOM	460	OD1	ASP	A	57	21.400	13.019	22.765	1.00	13.31	8
ATOM	461	OD2	ASP	A	57	23.391	13.058	23.622	1.00	17.36	8
ATOM	462	N	PHE	A	58	19.554	11.263	20.737	1.00	11.17	7
ATOM	463	CA	PHE	A	58	18.729	12.002	19.764	1.00	13.01	6
ATOM	464	C	PHE	A	58	18.675	13.475	20.055	1.00	16.32	6
ATOM	465	O	PHE	A	58	18.071	14.222	19.282	1.00	17.71	8

ATOM	466	CB	PHE	A	58	17.292	11.407	19.790	1.00	14.04	6
ATOM	467	CG	PHE	A	58	17.284	10.018	19.247	1.00	11.93	6
ATOM	468	CD1	PHE	A	58	17.055	9.878	17.861	1.00	12.43	6
ATOM	469	CD2	PHE	A	58	17.546	8.841	19.950	1.00	11.15	6
ATOM	470	CE1	PHE	A	58	17.078	8.627	17.325	1.00	13.41	6
ATOM	471	CE2	PHE	A	58	17.564	7.606	19.383	1.00	13.98	6
ATOM	472	CZ	PHE	A	58	17.345	7.456	17.990	1.00	12.24	6
ATOM	473	N	ILE	A	59	19.092	13.940	21.251	1.00	13.50	7
ATOM	474	CA	ILE	A	59	19.180	15.354	21.596	1.00	15.65	6
ATOM	475	C	ILE	A	59	20.410	15.974	20.964	1.00	18.12	6
ATOM	476	O	ILE	A	59	20.220	17.014	20.263	1.00	23.97	8
ATOM	477	CB	ILE	A	59	19.241	15.477	23.146	1.00	15.66	6
ATOM	478	CG1	ILE	A	59	17.951	15.100	23.855	1.00	19.46	6
ATOM	479	CG2	ILE	A	59	19.590	16.921	23.536	1.00	22.80	6
ATOM	480	CD1	ILE	A	59	16.626	15.695	23.499	1.00	21.33	6
ATOM	481	N	ASP	A	60	21.568	15.421	21.177	1.00	19.52	7
ATOM	482	CA	ASP	A	60	22.810	15.974	20.563	1.00	20.37	6
ATOM	483	C	ASP	A	60	23.051	15.391	19.176	1.00	23.56	6
ATOM	484	O	ASP	A	60	24.039	15.842	18.532	1.00	21.66	8
ATOM	485	CB	ASP	A	60	24.011	15.638	21.423	1.00	24.04	6
ATOM	486	CG	ASP	A	60	24.163	16.251	22.799	1.00	29.23	6
ATOM	487	OD1	ASP	A	60	23.498	17.279	23.093	1.00	27.86	8
ATOM	488	OD2	ASP	A	60	24.968	15.676	23.597	1.00	22.41	8
ATOM	489	N	ARG	A	61	22.353	14.341	18.772	1.00	18.93	7
ATOM	490	CA	ARG	A	61	22.668	13.639	17.519	1.00	18.74	6
ATOM	491	C	ARG	A	61	24.106	13.184	17.487	1.00	22.32	6
ATOM	492	O	ARG	A	61	25.042	13.415	16.667	1.00	20.82	8
ATOM	493	CB	ARG	A	61	22.241	14.566	16.363	1.00	20.03	6
ATOM	494	CG	ARG	A	61	20.743	14.751	16.239	1.00	27.06	6
ATOM	495	CD	ARG	A	61	20.210	15.689	15.210	0.00	20.00	6
ATOM	496	NE	ARG	A	61	19.042	16.306	15.859	0.00	20.00	7
ATOM	497	CZ	ARG	A	61	18.388	17.288	15.185	0.00	20.00	6
ATOM	498	NH1	ARG	A	61	18.805	17.666	13.981	0.00	20.00	7
ATOM	499	NH2	ARG	A	61	17.318	17.872	15.746	0.00	20.00	7
ATOM	500	N	ASP	A	62	24.436	12.342	18.480	1.00	18.53	7
ATOM	501	CA	ASP	A	62	25.742	11.759	18.713	1.00	19.28	6
ATOM	502	C	ASP	A	62	25.598	10.378	19.351	1.00	17.15	6
ATOM	503	O	ASP	A	62	24.462	9.943	19.708	1.00	17.25	8
ATOM	504	CB	ASP	A	62	26.663	12.711	19.495	1.00	19.71	6
ATOM	505	CG	ASP	A	62	26.330	12.887	20.966	1.00	25.11	6
ATOM	506	OD1	ASP	A	62	25.880	11.940	21.630	1.00	17.54	8
ATOM	507	OD2	ASP	A	62	26.480	13.999	21.532	1.00	26.53	8
ATOM	508	N	ASN	A	63	26.690	9.644	19.555	1.00	16.07	7
ATOM	509	CA	ASN	A	63	26.714	8.291	20.046	1.00	18.08	6
ATOM	510	C	ASN	A	63	27.071	8.238	21.540	1.00	14.21	6
ATOM	511	O	ASN	A	63	27.589	7.220	22.004	1.00	19.73	8
ATOM	512	CB	ASN	A	63	27.775	7.473	19.289	1.00	22.90	6
ATOM	513	CG	ASN	A	63	29.335	7.776	19.315	0.00	20.00	6
ATOM	514	OD1	ASN	A	63	30.201	6.934	19.572	0.00	20.00	8
ATOM	515	ND2	ASN	A	63	29.600	9.079	19.152	0.00	20.00	7
ATOM	516	N	ASN	A	64	26.975	9.391	22.182	1.00	15.25	7
ATOM	517	CA	ASN	A	64	27.400	9.532	23.602	1.00	16.89	6
ATOM	518	C	ASN	A	64	26.266	10.079	24.433	1.00	14.33	6
ATOM	519	O	ASN	A	64	25.999	11.262	24.588	1.00	14.56	8
ATOM	520	CB	ASN	A	64	28.546	10.586	23.613	1.00	16.40	6
ATOM	521	CG	ASN	A	64	29.073	10.797	25.019	1.00	20.17	6
ATOM	522	OD1	ASN	A	64	28.566	10.200	25.964	1.00	24.63	8
ATOM	523	ND2	ASN	A	64	30.049	11.702	25.183	1.00	24.89	7
ATOM	524	N	PRO	A	65	25.502	9.138	24.989	1.00	11.21	7
ATOM	525	CA	PRO	A	65	24.242	9.477	25.665	1.00	13.27	6
ATOM	526	C	PRO	A	65	24.437	9.812	27.151	1.00	13.67	6
ATOM	527	O	PRO	A	65	23.672	9.379	28.013	1.00	12.46	8
ATOM	528	CB	PRO	A	65	23.409	8.174	25.491	1.00	12.03	6
ATOM	529	CG	PRO	A	65	24.468	7.118	25.660	1.00	13.48	6
ATOM	530	CD	PRO	A	65	25.668	7.692	24.820	1.00	11.45	6
ATOM	531	N	MET	A	66	25.496	10.590	27.413	1.00	12.49	7
ATOM	532	CA	MET	A	66	25.738	11.074	28.772	1.00	10.69	6
ATOM	533	C	MET	A	66	24.601	11.947	29.263	1.00	10.89	6

ATOM	534	O	MET	A	66	23.929	12.691	28.560	1.00	12.73	8
ATOM	535	CB	MET	A	66	27.055	11.880	28.760	1.00	14.19	6
ATOM	536	CG	MET	A	66	27.469	12.471	30.079	1.00	13.14	6
ATOM	537	SD	MET	A	66	27.514	11.384	31.542	1.00	14.24	16
ATOM	538	CE	MET	A	66	28.725	10.247	30.960	1.00	16.73	6
ATOM	539	N	ASP	A	67	24.280	11.753	30.541	1.00	12.39	7
ATOM	540	CA	ASP	A	67	23.223	12.441	31.250	1.00	13.65	6
ATOM	541	C	ASP	A	67	23.622	13.848	31.714	1.00	13.30	6
ATOM	542	O	ASP	A	67	24.628	13.878	32.457	1.00	14.71	8
ATOM	543	CB	ASP	A	67	22.881	11.608	32.498	1.00	12.61	6
ATOM	544	CG	ASP	A	67	21.584	12.025	33.128	1.00	10.52	6
ATOM	545	OD1	ASP	A	67	20.838	12.937	32.766	1.00	10.71	8
ATOM	546	OD2	ASP	A	67	21.311	11.380	34.194	1.00	11.95	8
ATOM	547	N	LEU	A	68	22.901	14.887	31.398	1.00	12.91	7
ATOM	548	CA	LEU	A	68	23.230	16.219	31.935	1.00	11.29	6
ATOM	549	C	LEU	A	68	22.184	16.689	32.938	1.00	17.10	6
ATOM	550	O	LEU	A	68	21.977	17.877	33.191	1.00	18.88	8
ATOM	551	CB	LEU	A	68	23.273	17.220	30.784	1.00	13.93	6
ATOM	552	CG	LEU	A	68	24.425	16.942	29.829	1.00	18.76	6
ATOM	553	CD1	LEU	A	68	24.437	18.059	28.780	1.00	20.21	6
ATOM	554	CD2	LEU	A	68	25.787	16.856	30.516	1.00	23.79	6
ATOM	555	N	ASN	A	69	21.312	15.750	33.311	1.00	14.50	7
ATOM	556	CA	ASN	A	69	20.183	16.121	34.185	1.00	13.25	6
ATOM	557	C	ASN	A	69	20.208	15.373	35.507	1.00	15.28	6
ATOM	558	O	ASN	A	69	20.055	15.947	36.595	1.00	13.89	8
ATOM	559	CB	ASN	A	69	18.837	15.820	33.493	1.00	13.49	6
ATOM	560	CG	ASN	A	69	17.700	16.122	34.412	1.00	13.28	6
ATOM	561	OD1	ASN	A	69	17.292	15.258	35.220	1.00	15.35	8
ATOM	562	ND2	ASN	A	69	17.132	17.347	34.413	1.00	12.65	7
ATOM	563	N	GLY	A	70	20.371	14.062	35.389	1.00	11.32	7
ATOM	564	CA	GLY	A	70	20.428	13.126	36.501	1.00	12.47	6
ATOM	565	C	GLY	A	70	19.248	12.180	36.565	1.00	12.10	6
ATOM	566	O	GLY	A	70	19.392	11.092	37.153	1.00	11.37	8
ATOM	567	N	HIS	A	71	18.098	12.548	36.033	1.00	10.92	7
ATOM	568	CA	HIS	A	71	16.928	11.677	36.064	1.00	12.16	6
ATOM	569	C	HIS	A	71	17.178	10.320	35.425	1.00	10.47	6
ATOM	570	O	HIS	A	71	16.936	9.246	36.005	1.00	10.18	8
ATOM	571	CB	HIS	A	71	15.866	12.443	35.303	1.00	12.10	6
ATOM	572	CG	HIS	A	71	14.491	11.898	35.281	1.00	10.59	6
ATOM	573	ND1	HIS	A	71	14.070	11.083	34.222	1.00	9.81	7
ATOM	574	CD2	HIS	A	71	13.448	12.059	36.137	1.00	11.36	6
ATOM	575	CE1	HIS	A	71	12.804	10.755	34.481	1.00	9.45	6
ATOM	576	NE2	HIS	A	71	12.394	11.339	35.617	1.00	11.67	7
ATOM	577	N	GLY	A	72	17.747	10.309	34.214	1.00	9.91	7
ATOM	578	CA	GLY	A	72	17.985	9.019	33.539	1.00	8.20	6
ATOM	579	C	GLY	A	72	18.943	8.130	34.294	1.00	10.22	6
ATOM	580	O	GLY	A	72	18.851	6.914	34.210	1.00	11.25	8
ATOM	581	N	THR	A	73	19.996	8.710	34.949	1.00	9.41	7
ATOM	582	CA	THR	A	73	20.943	7.870	35.678	1.00	10.00	6
ATOM	583	C	THR	A	73	20.264	7.190	36.904	1.00	9.47	6
ATOM	584	O	THR	A	73	20.593	6.058	37.215	1.00	10.68	8
ATOM	585	CB	THR	A	73	22.092	8.789	36.140	1.00	12.41	6
ATOM	586	OG1	THR	A	73	22.771	9.288	34.942	1.00	11.16	8
ATOM	587	CG2	THR	A	73	23.170	8.096	36.950	1.00	11.66	6
ATOM	588	N	HIS	A	74	19.332	7.989	37.489	1.00	9.10	7
ATOM	589	CA	HIS	A	74	18.615	7.468	38.683	1.00	10.08	6
ATOM	590	C	HIS	A	74	17.725	6.317	38.222	1.00	8.45	6
ATOM	591	O	HIS	A	74	17.755	5.193	38.797	1.00	9.63	8
ATOM	592	CB	HIS	A	74	17.893	8.629	39.336	1.00	11.77	6
ATOM	593	CG	HIS	A	74	17.373	8.281	40.697	1.00	10.65	6
ATOM	594	ND1	HIS	A	74	16.237	7.546	40.892	1.00	10.09	7
ATOM	595	CD2	HIS	A	74	17.889	8.640	41.909	1.00	10.65	6
ATOM	596	CE1	HIS	A	74	16.057	7.418	42.194	1.00	10.71	6
ATOM	597	NE2	HIS	A	74	17.011	8.091	42.847	1.00	11.39	7
ATOM	598	N	VAL	A	75	16.991	6.560	37.128	1.00	8.72	7
ATOM	599	CA	VAL	A	75	16.102	5.516	36.601	1.00	9.96	6
ATOM	600	C	VAL	A	75	16.861	4.281	36.196	1.00	9.80	6
ATOM	601	O	VAL	A	75	16.493	3.159	36.569	1.00	9.73	8

ATOM	602	CB	VAL	A	75	15.368	6.143	35.397	1.00	8.91	6
ATOM	603	CG1	VAL	A	75	14.632	5.037	34.614	1.00	11.90	6
ATOM	604	CG2	VAL	A	75	14.373	7.207	35.906	1.00	12.26	6
ATOM	605	N	ALA	A	76	18.045	4.463	35.550	1.00	9.95	7
ATOM	606	CA	ALA	A	76	18.828	3.299	35.109	1.00	10.80	6
ATOM	607	C	ALA	A	76	19.311	2.512	36.325	1.00	8.05	6
ATOM	608	O	ALA	A	76	19.350	1.268	36.257	1.00	9.57	8
ATOM	609	CB	ALA	A	76	20.067	3.817	34.296	1.00	11.31	6
ATOM	610	N	GLY	A	77	19.719	3.244	37.394	1.00	8.67	7
ATOM	611	CA	GLY	A	77	20.240	2.442	38.509	1.00	10.66	6
ATOM	612	C	GLY	A	77	19.100	1.609	39.154	1.00	8.38	6
ATOM	613	O	GLY	A	77	19.432	0.501	39.628	1.00	9.24	8
ATOM	614	N	THR	A	78	17.898	2.146	39.196	1.00	8.84	7
ATOM	615	CA	THR	A	78	16.820	1.294	39.724	1.00	9.31	6
ATOM	616	C	THR	A	78	16.604	0.018	38.930	1.00	7.59	6
ATOM	617	O	THR	A	78	16.379	-1.093	39.396	1.00	10.79	8
ATOM	618	CB	THR	A	78	15.550	2.127	39.833	1.00	9.05	6
ATOM	619	OG1	THR	A	78	15.760	3.175	40.796	1.00	10.11	8
ATOM	620	CG2	THR	A	78	14.375	1.266	40.327	1.00	10.42	6
ATOM	621	N	VAL	A	79	16.642	0.189	37.555	1.00	9.12	7
ATOM	622	CA	VAL	A	79	16.411	-0.985	36.685	1.00	8.17	6
ATOM	623	C	VAL	A	79	17.466	-2.025	36.875	1.00	8.18	6
ATOM	624	O	VAL	A	79	17.192	-3.196	36.970	1.00	10.26	8
ATOM	625	CB	VAL	A	79	16.354	-0.577	35.186	1.00	13.01	6
ATOM	626	CG1	VAL	A	79	16.039	-1.862	34.342	1.00	16.27	6
ATOM	627	CG2	VAL	A	79	15.250	0.388	34.873	1.00	16.24	6
ATOM	628	N	ALA	A	80	18.753	-1.594	36.861	1.00	9.76	7
ATOM	629	CA	ALA	A	80	19.799	-2.612	36.679	1.00	9.95	6
ATOM	630	C	ALA	A	80	21.149	-2.084	37.067	1.00	11.86	6
ATOM	631	O	ALA	A	80	22.196	-2.334	36.405	1.00	10.30	8
ATOM	632	CB	ALA	A	80	19.814	-3.107	35.195	1.00	10.99	6
ATOM	633	N	ALA	A	81	21.287	-1.333	38.172	1.00	10.11	7
ATOM	634	CA	ALA	A	81	22.606	-1.043	38.738	1.00	8.94	6
ATOM	635	C	ALA	A	81	23.431	-2.334	38.881	1.00	10.93	6
ATOM	636	O	ALA	A	81	22.877	-3.375	39.066	1.00	10.46	8
ATOM	637	CB	ALA	A	81	22.577	-0.382	40.119	1.00	8.60	6
ATOM	638	N	ASP	A	82	24.767	-2.153	38.897	1.00	9.68	7
ATOM	639	CA	ASP	A	82	25.667	-3.283	39.195	1.00	13.33	6
ATOM	640	C	ASP	A	82	25.333	-3.770	40.643	1.00	9.64	6
ATOM	641	O	ASP	A	82	25.341	-2.891	41.492	1.00	10.48	8
ATOM	642	CB	ASP	A	82	27.068	-2.744	39.036	1.00	11.80	6
ATOM	643	CG	ASP	A	82	28.160	-3.765	38.888	1.00	13.40	6
ATOM	644	OD1	ASP	A	82	29.241	-3.350	38.394	1.00	12.00	8
ATOM	645	OD2	ASP	A	82	27.952	-4.901	39.318	1.00	12.74	8
ATOM	646	N	THR	A	83	25.143	-5.049	40.755	1.00	9.60	7
ATOM	647	CA	THR	A	83	24.598	-5.567	42.041	1.00	10.59	6
ATOM	648	C	THR	A	83	25.509	-6.677	42.574	1.00	11.19	6
ATOM	649	O	THR	A	83	26.203	-7.421	41.875	1.00	13.87	8
ATOM	650	CB	THR	A	83	23.240	-6.205	41.715	1.00	12.73	6
ATOM	651	OG1	THR	A	83	22.452	-5.144	41.178	1.00	11.10	8
ATOM	652	CG2	THR	A	83	22.502	-6.829	42.913	1.00	11.07	6
ATOM	653	N	ASN	A	84	25.558	-6.640	43.926	1.00	11.01	7
ATOM	654	CA	ASN	A	84	26.421	-7.579	44.672	1.00	12.42	6
ATOM	655	C	ASN	A	84	27.916	-7.260	44.404	1.00	12.70	6
ATOM	656	O	ASN	A	84	28.717	-8.171	44.505	1.00	14.84	8
ATOM	657	CB	ASN	A	84	26.083	-9.024	44.364	1.00	14.55	6
ATOM	658	CG	ASN	A	84	26.516	-9.910	45.538	1.00	17.95	6
ATOM	659	OD1	ASN	A	84	26.308	-9.587	46.712	1.00	16.26	8
ATOM	660	ND2	ASN	A	84	27.136	-11.035	45.221	1.00	19.28	7
ATOM	661	N	ASN	A	85	28.181	-5.973	44.137	1.00	11.37	7
ATOM	662	CA	ASN	A	85	29.540	-5.534	43.883	1.00	11.85	6
ATOM	663	C	ASN	A	85	30.208	-4.745	44.988	1.00	11.88	6
ATOM	664	O	ASN	A	85	31.195	-4.054	44.863	1.00	14.14	8
ATOM	665	CB	ASN	A	85	29.614	-4.736	42.574	1.00	12.33	6
ATOM	666	CG	ASN	A	85	28.901	-3.418	42.600	1.00	12.64	6
ATOM	667	OD1	ASN	A	85	27.959	-3.237	43.365	1.00	11.43	8
ATOM	668	ND2	ASN	A	85	29.298	-2.439	41.789	1.00	11.56	7
ATOM	669	N	GLY	A	86	29.539	-4.755	46.163	1.00	12.16	7

ATOM	670	CA	GLY	A	86	29.982	-4.130	47.358	1.00	12.38	6
ATOM	671	C	GLY	A	86	30.003	-2.614	47.377	1.00	14.42	6
ATOM	672	O	GLY	A	86	30.591	-1.914	48.220	1.00	18.31	8
ATOM	673	N	ILE	A	87	29.329	-2.004	46.388	1.00	12.81	7
ATOM	674	CA	ILE	A	87	29.278	-0.603	46.104	1.00	11.71	6
ATOM	675	C	ILE	A	87	27.805	-0.195	45.920	1.00	10.49	6
ATOM	676	O	ILE	A	87	27.039	-0.898	45.250	1.00	11.65	8
ATOM	677	CB	ILE	A	87	30.001	-0.268	44.734	1.00	13.16	6
ATOM	678	CG1	ILE	A	87	31.488	-0.601	44.998	1.00	15.49	6
ATOM	679	CG2	ILE	A	87	29.743	1.152	44.317	1.00	17.65	6
ATOM	680	CD1	ILE	A	87	32.209	-0.655	43.631	1.00	17.42	6
ATOM	681	N	GLY	A	88	27.452	0.954	46.442	1.00	12.42	7
ATOM	682	CA	GLY	A	88	26.194	1.569	45.989	1.00	11.25	6
ATOM	683	C	GLY	A	88	24.950	0.749	46.250	1.00	9.96	6
ATOM	684	O	GLY	A	88	24.668	0.199	47.288	1.00	11.18	8
ATOM	685	N	VAL	A	89	24.106	0.667	45.193	1.00	10.48	7
ATOM	686	CA	VAL	A	89	22.741	0.149	45.260	1.00	8.53	6
ATOM	687	C	VAL	A	89	22.639	-1.190	44.549	1.00	11.23	6
ATOM	688	O	VAL	A	89	23.666	-1.596	43.948	1.00	10.26	8
ATOM	689	CB	VAL	A	89	21.727	1.175	44.689	1.00	10.06	6
ATOM	690	CG1	VAL	A	89	21.615	2.398	45.639	1.00	11.70	6
ATOM	691	CG2	VAL	A	89	22.081	1.654	43.263	1.00	10.54	6
ATOM	692	N	ALA	A	90	21.477	-1.829	44.640	1.00	7.95	7
ATOM	693	CA	ALA	A	90	21.184	-3.046	43.869	1.00	8.13	6
ATOM	694	C	ALA	A	90	20.078	-2.755	42.876	1.00	8.97	6
ATOM	695	O	ALA	A	90	19.085	-2.156	43.204	1.00	10.80	8
ATOM	696	CB	ALA	A	90	20.696	-4.124	44.835	1.00	11.49	6
ATOM	697	N	GLY	A	91	20.356	-3.266	41.655	1.00	9.50	7
ATOM	698	CA	GLY	A	91	19.313	-3.059	40.624	1.00	10.29	6
ATOM	699	C	GLY	A	91	18.278	-4.178	40.615	1.00	10.12	6
ATOM	700	O	GLY	A	91	18.457	-5.295	41.120	1.00	9.70	8
ATOM	701	N	MET	A	92	17.069	-3.849	40.120	1.00	10.51	7
ATOM	702	CA	MET	A	92	15.995	-4.836	40.046	1.00	10.40	6
ATOM	703	C	MET	A	92	16.312	-6.044	39.169	1.00	8.63	6
ATOM	704	O	MET	A	92	15.853	-7.173	39.474	1.00	10.07	8
ATOM	705	CB	MET	A	92	14.700	-4.133	39.525	1.00	10.66	6
ATOM	706	CG	MET	A	92	14.024	-3.346	40.670	1.00	10.45	6
ATOM	707	SD	MET	A	92	13.253	-4.371	41.946	1.00	11.55	16
ATOM	708	CE	MET	A	92	11.912	-5.093	41.007	1.00	12.16	6
ATOM	709	N	ALA	A	93	17.126	-5.840	38.098	1.00	8.87	7
ATOM	710	CA	ALA	A	93	17.598	-6.935	37.268	1.00	10.60	6
ATOM	711	C	ALA	A	93	19.126	-6.945	37.275	1.00	12.63	6
ATOM	712	O	ALA	A	93	19.803	-6.326	36.467	1.00	11.07	8
ATOM	713	CB	ALA	A	93	17.041	-6.652	35.841	1.00	11.23	6
ATOM	714	N	PRO	A	94	19.692	-7.579	38.287	1.00	10.81	7
ATOM	715	CA	PRO	A	94	21.127	-7.515	38.517	1.00	12.42	6
ATOM	716	C	PRO	A	94	21.963	-7.765	37.291	1.00	12.53	6
ATOM	717	O	PRO	A	94	22.990	-7.094	37.087	1.00	14.34	8
ATOM	718	CB	PRO	A	94	21.350	-8.634	39.578	1.00	11.90	6
ATOM	719	CG	PRO	A	94	20.077	-8.538	40.360	1.00	12.96	6
ATOM	720	CD	PRO	A	94	18.941	-8.272	39.338	1.00	12.20	6
ATOM	721	N	ASP	A	95	21.647	-8.786	36.456	1.00	11.92	7
ATOM	722	CA	ASP	A	95	22.593	-9.148	35.399	1.00	11.78	6
ATOM	723	C	ASP	A	95	22.215	-8.578	34.037	1.00	12.73	6
ATOM	724	O	ASP	A	95	23.039	-8.643	33.127	1.00	14.73	8
ATOM	725	CB	ASP	A	95	22.661	-10.672	35.300	1.00	12.28	6
ATOM	726	CG	ASP	A	95	23.335	-11.242	36.572	1.00	18.00	6
ATOM	727	OD1	ASP	A	95	24.147	-10.496	37.098	1.00	20.06	8
ATOM	728	OD2	ASP	A	95	22.929	-12.386	36.860	1.00	27.51	8
ATOM	729	N	THR	A	96	21.016	-7.956	33.957	1.00	12.12	7
ATOM	730	CA	THR	A	96	20.613	-7.407	32.635	1.00	12.08	6
ATOM	731	C	THR	A	96	21.336	-6.110	32.325	1.00	11.03	6
ATOM	732	O	THR	A	96	21.555	-5.271	33.207	1.00	12.04	8
ATOM	733	CB	THR	A	96	19.095	-7.274	32.590	1.00	10.42	6
ATOM	734	OG1	THR	A	96	18.501	-8.585	32.725	1.00	12.83	8
ATOM	735	CG2	THR	A	96	18.523	-6.733	31.241	1.00	11.86	6
ATOM	736	N	LYS	A	97	21.685	-5.929	31.026	1.00	10.74	7
ATOM	737	CA	LYS	A	97	22.392	-4.675	30.685	1.00	11.13	6

ATOM	738	C	LYS	A	97	21.400	-3.550	30.376	1.00	12.38	6
ATOM	739	O	LYS	A	97	20.182	-3.832	30.148	1.00	11.36	8
ATOM	740	CB	ALYS	A	97	23.198	-4.880	29.382	0.50	12.99	6
ATOM	741	CG	ALYS	A	97	24.181	-6.046	29.425	0.50	17.25	6
ATOM	742	CD	ALYS	A	97	25.152	-5.891	30.584	0.50	15.11	6
ATOM	743	CE	ALYS	A	97	26.500	-6.533	30.211	0.50	12.42	6
ATOM	744	NZ	ALYS	A	97	27.416	-6.547	31.382	0.50	18.98	7
ATOM	745	CB	BLYS	A	97	23.436	-4.843	29.571	0.50	14.58	6
ATOM	746	CG	BLYS	A	97	24.588	-5.769	29.995	0.50	15.40	6
ATOM	747	CD	BLYS	A	97	25.597	-5.958	28.888	0.50	16.62	6
ATOM	748	CE	BLYS	A	97	26.770	-6.845	29.293	0.50	22.87	6
ATOM	749	NZ	BLYS	A	97	27.610	-6.168	30.320	0.50	27.60	7
ATOM	750	N	ILE	A	98	21.861	-2.310	30.465	1.00	10.38	7
ATOM	751	CA	ILE	A	98	21.048	-1.145	30.182	1.00	10.34	6
ATOM	752	C	ILE	A	98	21.459	-0.617	28.815	1.00	10.92	6
ATOM	753	O	ILE	A	98	22.618	-0.354	28.624	1.00	12.98	8
ATOM	754	CB	ILE	A	98	21.342	-0.073	31.253	1.00	10.78	6
ATOM	755	CG1	ILE	A	98	20.779	-0.412	32.644	1.00	11.69	6
ATOM	756	CG2	ILE	A	98	20.758	1.269	30.847	1.00	11.52	6
ATOM	757	CD1	ILE	A	98	21.604	0.253	33.746	1.00	14.34	6
ATOM	758	N	LEU	A	99	20.522	-0.415	27.892	1.00	9.93	7
ATOM	759	CA	LEU	A	99	20.815	0.298	26.649	1.00	10.06	6
ATOM	760	C	LEU	A	99	20.432	1.743	26.901	1.00	10.51	6
ATOM	761	O	LEU	A	99	19.225	2.085	27.071	1.00	9.69	8
ATOM	762	CB	LEU	A	99	19.984	-0.359	25.506	1.00	11.55	6
ATOM	763	CG	LEU	A	99	20.103	0.469	24.236	1.00	11.50	6
ATOM	764	CD1	LEU	A	99	21.553	0.416	23.750	1.00	12.90	6
ATOM	765	CD2	LEU	A	99	19.138	-0.039	23.204	1.00	10.92	6
ATOM	766	N	ALA	A	100	21.356	2.645	27.040	1.00	10.31	7
ATOM	767	CA	ALA	A	100	21.060	4.046	27.338	1.00	9.78	6
ATOM	768	C	ALA	A	100	20.713	4.770	26.039	1.00	9.48	6
ATOM	769	O	ALA	A	100	21.557	4.833	25.119	1.00	11.85	8
ATOM	770	CB	ALA	A	100	22.296	4.739	27.974	1.00	11.54	6
ATOM	771	N	VAL	A	101	19.480	5.268	26.012	1.00	9.16	7
ATOM	772	CA	VAL	A	101	19.062	6.013	24.795	1.00	10.09	6
ATOM	773	C	VAL	A	101	18.654	7.409	25.253	1.00	10.39	6
ATOM	774	O	VAL	A	101	17.733	7.523	26.060	1.00	9.86	8
ATOM	775	CB	VAL	A	101	17.937	5.305	24.085	1.00	10.01	6
ATOM	776	CG1	VAL	A	101	17.556	6.021	22.742	1.00	11.37	6
ATOM	777	CG2	VAL	A	101	18.227	3.846	23.765	1.00	12.69	6
ATOM	778	N	ARG	A	102	19.294	8.449	24.771	1.00	10.96	7
ATOM	779	CA	ARG	A	102	19.041	9.797	25.252	1.00	10.28	6
ATOM	780	C	ARG	A	102	18.003	10.499	24.396	1.00	13.39	6
ATOM	781	O	ARG	A	102	18.193	10.765	23.188	1.00	14.69	8
ATOM	782	CB	ARG	A	102	20.353	10.595	25.469	1.00	11.23	6
ATOM	783	CG	ARG	A	102	19.993	12.026	25.927	1.00	11.92	6
ATOM	784	CD	ARG	A	102	21.318	12.674	26.332	1.00	11.26	6
ATOM	785	NE	ARG	A	102	21.088	13.998	26.872	1.00	13.14	7
ATOM	786	CZ	ARG	A	102	21.537	15.160	26.462	1.00	17.86	6
ATOM	787	NH1	ARG	A	102	22.286	15.196	25.353	1.00	17.29	7
ATOM	788	NH2	ARG	A	102	21.231	16.264	27.119	1.00	13.78	7
ATOM	789	N	VAL	A	103	16.871	10.780	24.968	1.00	11.62	7
ATOM	790	CA	VAL	A	103	15.757	11.445	24.301	1.00	11.54	6
ATOM	791	C	VAL	A	103	15.264	12.696	25.053	1.00	12.58	6
ATOM	792	O	VAL	A	103	14.272	13.343	24.613	1.00	15.25	8
ATOM	793	CB	VAL	A	103	14.520	10.520	24.049	1.00	12.23	6
ATOM	794	CG1	VAL	A	103	14.893	9.393	23.047	1.00	15.01	6
ATOM	795	CG2	VAL	A	103	13.912	9.972	25.323	1.00	14.01	6
ATOM	796	N	LEU	A	104	15.806	13.018	26.201	1.00	13.17	7
ATOM	797	CA	LEU	A	104	15.505	14.207	26.989	1.00	13.95	6
ATOM	798	C	LEU	A	104	16.824	14.933	27.248	1.00	11.06	6
ATOM	799	O	LEU	A	104	17.900	14.395	27.389	1.00	12.49	8
ATOM	800	CB	LEU	A	104	14.908	13.887	28.361	1.00	16.60	6
ATOM	801	CG	LEU	A	104	13.683	12.967	28.283	1.00	12.90	6
ATOM	802	CD1	LEU	A	104	13.236	12.655	29.717	1.00	15.91	6
ATOM	803	CD2	LEU	A	104	12.590	13.532	27.433	1.00	17.02	6
ATOM	804	N	ASP	A	105	16.640	16.297	27.188	1.00	14.57	7
ATOM	805	CA	ASP	A	105	17.795	17.210	27.308	1.00	11.73	6

ATOM	806	C	ASP	A	105	18.165	17.499	28.737	1.00	14.97	6
ATOM	807	O	ASP	A	105	17.755	16.820	29.654	1.00	13.31	8
ATOM	808	CB	ASP	A	105	17.447	18.495	26.529	1.00	15.08	6
ATOM	809	CG	ASP	A	105	16.415	19.378	27.163	1.00	21.30	6
ATOM	810	OD1	ASP	A	105	16.024	19.199	28.320	1.00	16.65	8
ATOM	811	OD2	ASP	A	105	15.940	20.341	26.470	1.00	22.26	8
ATOM	812	N	ALA	A	106	19.112	18.442	28.926	1.00	15.23	7
ATOM	813	CA	ALA	A	106	19.549	18.691	30.304	1.00	13.88	6
ATOM	814	C	ALA	A	106	18.448	19.148	31.242	1.00	14.07	6
ATOM	815	O	ALA	A	106	18.632	18.970	32.464	1.00	15.73	8
ATOM	816	CB	ALA	A	106	20.623	19.791	30.277	1.00	16.83	6
ATOM	817	N	ASN	A	107	17.337	19.694	30.787	1.00	15.93	7
ATOM	818	CA	ASN	A	107	16.227	20.076	31.629	1.00	18.54	6
ATOM	819	C	ASN	A	107	15.139	19.031	31.736	1.00	17.24	6
ATOM	820	O	ASN	A	107	14.093	19.274	32.355	1.00	19.75	8
ATOM	821	CB	ASN	A	107	15.587	21.347	31.038	1.00	23.46	6
ATOM	822	CG	ASN	A	107	16.601	22.481	31.051	1.00	26.78	6
ATOM	823	OD1	ASN	A	107	17.162	22.753	32.113	1.00	25.51	8
ATOM	824	ND2	ASN	A	107	16.820	23.099	29.904	1.00	26.59	7
ATOM	825	N	GLY	A	108	15.389	17.863	31.134	1.00	16.72	7
ATOM	826	CA	GLY	A	108	14.401	16.793	31.185	1.00	19.02	6
ATOM	827	C	GLY	A	108	13.346	16.911	30.090	1.00	19.28	6
ATOM	828	O	GLY	A	108	12.324	16.199	30.201	1.00	23.96	8
ATOM	829	N	SER	A	109	13.569	17.695	29.071	1.00	18.97	7
ATOM	830	CA	SER	A	109	12.556	17.941	28.046	1.00	19.93	6
ATOM	831	C	SER	A	109	12.936	17.281	26.738	1.00	19.26	6
ATOM	832	O	SER	A	109	14.111	17.132	26.434	1.00	16.92	8
ATOM	833	CB	SER	A	109	12.425	19.456	27.829	1.00	27.39	6
ATOM	834	OG	SER	A	109	12.017	20.008	29.076	1.00	36.14	8
ATOM	835	N	GLY	A	110	11.937	16.950	25.927	1.00	19.72	7
ATOM	836	CA	GLY	A	110	12.225	16.262	24.673	1.00	20.18	6
ATOM	837	C	GLY	A	110	11.058	16.418	23.718	1.00	21.15	6
ATOM	838	O	GLY	A	110	9.991	16.848	24.138	1.00	27.11	8
ATOM	839	N	SER	A	111	11.377	16.282	22.422	1.00	16.93	7
ATOM	840	CA	SER	A	111	10.303	16.416	21.451	1.00	18.93	6
ATOM	841	C	SER	A	111	9.655	15.052	21.244	1.00	17.00	6
ATOM	842	O	SER	A	111	10.258	14.004	21.422	1.00	17.14	8
ATOM	843	CB	SER	A	111	10.853	16.982	20.148	1.00	21.62	6
ATOM	844	OG	SER	A	111	11.640	16.039	19.448	1.00	23.26	8
ATOM	845	N	LEU	A	112	8.354	15.122	20.969	1.00	16.14	7
ATOM	846	CA	LEU	A	112	7.698	13.807	20.756	1.00	15.65	6
ATOM	847	C	LEU	A	112	8.360	13.083	19.577	1.00	14.33	6
ATOM	848	O	LEU	A	112	8.393	11.832	19.644	1.00	17.13	8
ATOM	849	CB	LEU	A	112	6.187	13.940	20.629	1.00	21.81	6
ATOM	850	CG	LEU	A	112	5.437	14.470	21.857	1.00	22.13	6
ATOM	851	CD1	LEU	A	112	3.926	14.464	21.622	1.00	28.11	6
ATOM	852	CD2	LEU	A	112	5.685	13.699	23.153	1.00	25.27	6
ATOM	853	N	ASP	A	113	8.726	13.761	18.498	1.00	17.80	7
ATOM	854	CA	ASP	A	113	9.300	12.973	17.388	1.00	18.50	6
ATOM	855	C	ASP	A	113	10.622	12.343	17.758	1.00	19.37	6
ATOM	856	O	ASP	A	113	10.820	11.187	17.316	1.00	18.50	8
ATOM	857	CB	ASP	A	113	9.322	13.894	16.160	1.00	20.24	6
ATOM	858	CG	ASP	A	113	8.011	14.173	15.519	1.00	19.59	6
ATOM	859	OD1	ASP	A	113	7.995	15.140	14.672	1.00	29.00	8
ATOM	860	OD2	ASP	A	113	6.943	13.587	15.713	1.00	24.47	8
ATOM	861	N	SER	A	114	11.438	12.963	18.569	1.00	17.25	7
ATOM	862	CA	SER	A	114	12.699	12.385	19.032	1.00	20.51	6
ATOM	863	C	SER	A	114	12.440	11.230	19.998	1.00	17.38	6
ATOM	864	O	SER	A	114	13.134	10.212	19.896	1.00	16.74	8
ATOM	865	CB	SER	A	114	13.525	13.459	19.733	1.00	25.71	6
ATOM	866	OG	SER	A	114	14.016	14.313	18.706	1.00	28.28	8
ATOM	867	N	ILE	A	115	11.470	11.380	20.891	1.00	13.42	7
ATOM	868	CA	ILE	A	115	11.184	10.283	21.816	1.00	11.54	6
ATOM	869	C	ILE	A	115	10.687	9.106	21.001	1.00	11.78	6
ATOM	870	O	ILE	A	115	11.072	7.934	21.265	1.00	12.76	8
ATOM	871	CB	ILE	A	115	10.132	10.720	22.855	1.00	12.31	6
ATOM	872	CG1	ILE	A	115	10.815	11.775	23.737	1.00	15.30	6
ATOM	873	CG2	ILE	A	115	9.621	9.579	23.726	1.00	14.78	6

ATOM	874	CD1	ILE	A	115	9.771	12.522	24.544	1.00	16.55	6
ATOM	875	N	ALA	A	116	9.807	9.353	20.024	1.00	12.41	7
ATOM	876	CA	ALA	A	116	9.318	8.291	19.178	1.00	11.46	6
ATOM	877	C	ALA	A	116	10.435	7.610	18.400	1.00	10.70	6
ATOM	878	O	ALA	A	116	10.537	6.377	18.397	1.00	11.22	8
ATOM	879	CB	ALA	A	116	8.292	8.902	18.184	1.00	14.75	6
ATOM	880	N	SER	A	117	11.370	8.395	17.848	1.00	12.15	7
ATOM	881	CA	SER	A	117	12.490	7.738	17.150	1.00	12.96	6
ATOM	882	C	SER	A	117	13.387	6.913	18.093	1.00	10.71	6
ATOM	883	O	SER	A	117	13.805	5.814	17.704	1.00	13.52	8
ATOM	884	CB	SER	A	117	13.345	8.825	16.510	1.00	15.02	6
ATOM	885	OG	SER	A	117	12.600	9.369	15.405	1.00	17.64	8
ATOM	886	N	GLY	A	118	13.537	7.392	19.343	1.00	11.17	7
ATOM	887	CA	GLY	A	118	14.357	6.612	20.301	1.00	11.65	6
ATOM	888	C	GLY	A	118	13.617	5.336	20.707	1.00	12.79	6
ATOM	889	O	GLY	A	118	14.241	4.305	20.887	1.00	11.77	8
ATOM	890	N	ILE	A	119	12.284	5.358	20.869	1.00	10.37	7
ATOM	891	CA	ILE	A	119	11.517	4.140	21.164	1.00	9.25	6
ATOM	892	C	ILE	A	119	11.754	3.131	20.016	1.00	9.88	6
ATOM	893	O	ILE	A	119	11.966	1.949	20.317	1.00	9.88	8
ATOM	894	CB	ILE	A	119	10.045	4.484	21.337	1.00	8.90	6
ATOM	895	CG1	ILE	A	119	9.871	5.274	22.714	1.00	10.96	6
ATOM	896	CG2	ILE	A	119	9.131	3.264	21.306	1.00	10.98	6
ATOM	897	CD1	ILE	A	119	8.439	5.822	22.768	1.00	11.18	6
ATOM	898	N	ARG	A	120	11.557	3.597	18.756	1.00	9.24	7
ATOM	899	CA	ARG	A	120	11.799	2.616	17.683	1.00	10.97	6
ATOM	900	C	ARG	A	120	13.239	2.125	17.652	1.00	9.58	6
ATOM	901	O	ARG	A	120	13.447	0.905	17.482	1.00	11.11	8
ATOM	902	CB	ARG	A	120	11.497	3.354	16.336	1.00	10.45	6
ATOM	903	CG	ARG	A	120	10.021	3.739	16.215	1.00	12.73	6
ATOM	904	CD	ARG	A	120	9.770	4.717	14.988	1.00	12.77	6
ATOM	905	NE	ARG	A	120	9.824	3.724	13.911	1.00	13.28	7
ATOM	906	CZ	ARG	A	120	8.753	3.068	13.512	1.00	11.79	6
ATOM	907	NH1	ARG	A	120	7.523	3.292	13.896	1.00	12.69	7
ATOM	908	NH2	ARG	A	120	8.965	2.095	12.638	1.00	11.60	7
ATOM	909	N	TYR	A	121	14.187	3.005	17.934	1.00	10.24	7
ATOM	910	CA	TYR	A	121	15.594	2.588	17.988	1.00	12.90	6
ATOM	911	C	TYR	A	121	15.860	1.471	18.969	1.00	9.83	6
ATOM	912	O	TYR	A	121	16.522	0.447	18.788	1.00	11.54	8
ATOM	913	CB	TYR	A	121	16.416	3.837	18.292	1.00	12.06	6
ATOM	914	CG	TYR	A	121	17.853	3.571	18.596	1.00	11.82	6
ATOM	915	CD1	TYR	A	121	18.818	3.475	17.604	1.00	13.12	6
ATOM	916	CD2	TYR	A	121	18.273	3.395	19.896	1.00	11.97	6
ATOM	917	CE1	TYR	A	121	20.157	3.225	17.930	1.00	13.85	6
ATOM	918	CE2	TYR	A	121	19.575	3.177	20.250	1.00	11.79	6
ATOM	919	CZ	TYR	A	121	20.518	3.073	19.252	1.00	15.08	6
ATOM	920	OH	TYR	A	121	21.856	2.849	19.585	1.00	17.95	8
ATOM	921	N	ALA	A	122	15.231	1.676	20.166	1.00	9.11	7
ATOM	922	CA	ALA	A	122	15.446	0.670	21.197	1.00	9.16	6
ATOM	923	C	ALA	A	122	14.894	-0.675	20.774	1.00	10.24	6
ATOM	924	O	ALA	A	122	15.500	-1.733	21.045	1.00	12.08	8
ATOM	925	CB	ALA	A	122	14.726	1.101	22.481	1.00	10.97	6
ATOM	926	N	ALA	A	123	13.672	-0.746	20.160	1.00	10.00	7
ATOM	927	CA	ALA	A	123	13.177	-2.032	19.660	1.00	9.79	6
ATOM	928	C	ALA	A	123	14.082	-2.548	18.522	1.00	10.77	6
ATOM	929	O	ALA	A	123	14.298	-3.791	18.464	1.00	12.07	8
ATOM	930	CB	ALA	A	123	11.747	-1.789	19.135	1.00	12.17	6
ATOM	931	N	ASP	A	124	14.513	-1.608	17.684	1.00	10.69	7
ATOM	932	CA	ASP	A	124	15.338	-2.079	16.548	1.00	11.25	6
ATOM	933	C	ASP	A	124	16.699	-2.611	17.014	1.00	11.36	6
ATOM	934	O	ASP	A	124	17.263	-3.536	16.372	1.00	12.55	8
ATOM	935	CB	ASP	A	124	15.528	-0.967	15.527	1.00	10.62	6
ATOM	936	CG	ASP	A	124	14.197	-0.704	14.727	1.00	11.72	6
ATOM	937	OD1	ASP	A	124	13.461	-1.679	14.609	1.00	13.58	8
ATOM	938	OD2	ASP	A	124	14.060	0.480	14.352	1.00	13.00	8
ATOM	939	N	GLN	A	125	17.178	-2.140	18.152	1.00	10.69	7
ATOM	940	CA	GLN	A	125	18.385	-2.681	18.772	1.00	11.00	6
ATOM	941	C	GLN	A	125	18.156	-3.958	19.527	1.00	10.13	6

ATOM	942	O	GLN	A	125	19.112	-4.519	20.114	1.00	14.93	8
ATOM	943	CB	GLN	A	125	19.045	-1.632	19.690	1.00	13.56	6
ATOM	944	CG	GLN	A	125	19.636	-0.472	18.900	1.00	15.15	6
ATOM	945	CD	GLN	A	125	20.953	-0.735	18.192	1.00	21.96	6
ATOM	946	OE1	GLN	A	125	21.571	-1.784	18.291	1.00	28.15	8
ATOM	947	NE2	GLN	A	125	21.464	0.234	17.433	1.00	29.01	7
ATOM	948	N	GLY	A	126	16.930	-4.457	19.666	1.00	9.97	7
ATOM	949	CA	GLY	A	126	16.710	-5.768	20.279	1.00	11.91	6
ATOM	950	C	GLY	A	126	16.402	-5.656	21.789	1.00	9.69	6
ATOM	951	O	GLY	A	126	16.461	-6.756	22.347	1.00	11.42	8
ATOM	952	N	ALA	A	127	16.191	-4.473	22.311	1.00	10.80	7
ATOM	953	CA	ALA	A	127	15.916	-4.514	23.775	1.00	11.01	6
ATOM	954	C	ALA	A	127	14.656	-5.298	24.094	1.00	11.87	6
ATOM	955	O	ALA	A	127	13.625	-5.169	23.382	1.00	11.59	8
ATOM	956	CB	ALA	A	127	15.812	-3.046	24.241	1.00	11.61	6
ATOM	957	N	LYS	A	128	14.714	-6.115	25.193	1.00	10.72	7
ATOM	958	CA	LYS	A	128	13.507	-6.851	25.520	1.00	10.65	6
ATOM	959	C	LYS	A	128	12.450	-6.045	26.274	1.00	8.78	6
ATOM	960	O	LYS	A	128	11.270	-6.377	26.201	1.00	10.35	8
ATOM	961	CB	LYS	A	128	13.834	-8.046	26.442	1.00	12.01	6
ATOM	962	CG	LYS	A	128	14.845	-9.003	25.841	1.00	17.41	6
ATOM	963	CD	LYS	A	128	14.181	-9.713	24.663	1.00	17.61	6
ATOM	964	CE	LYS	A	128	15.182	-10.781	24.174	1.00	24.85	6
ATOM	965	NZ	LYS	A	128	14.810	-11.333	22.835	1.00	23.69	7
ATOM	966	N	VAL	A	129	12.912	-4.970	26.905	1.00	9.09	7
ATOM	967	CA	VAL	A	129	12.007	-4.094	27.687	1.00	8.78	6
ATOM	968	C	VAL	A	129	12.468	-2.678	27.406	1.00	8.25	6
ATOM	969	O	VAL	A	129	13.664	-2.390	27.317	1.00	10.23	8
ATOM	970	CB	VAL	A	129	12.239	-4.362	29.188	1.00	10.07	6
ATOM	971	CG1	VAL	A	129	11.286	-3.527	30.071	1.00	10.09	6
ATOM	972	CG2	VAL	A	129	11.977	-5.856	29.468	1.00	10.08	6
ATOM	973	N	LEU	A	130	11.489	-1.779	27.289	1.00	8.25	7
ATOM	974	CA	LEU	A	130	11.736	-0.350	27.185	1.00	8.42	6
ATOM	975	C	LEU	A	130	11.104	0.353	28.411	1.00	8.00	6
ATOM	976	O	LEU	A	130	9.952	0.083	28.784	1.00	9.41	8
ATOM	977	CB	LEU	A	130	11.008	0.264	25.940	1.00	11.97	6
ATOM	978	CG	LEU	A	130	11.719	0.108	24.579	1.00	10.92	6
ATOM	979	CD1	LEU	A	130	11.814	-1.346	24.191	1.00	13.24	6
ATOM	980	CD2	LEU	A	130	10.890	0.862	23.514	1.00	10.28	6
ATOM	981	N	ASN	A	131	11.941	1.213	29.065	1.00	7.78	7
ATOM	982	CA	ASN	A	131	11.363	1.989	30.168	1.00	8.96	6
ATOM	983	C	ASN	A	131	11.240	3.469	29.713	1.00	9.31	6
ATOM	984	O	ASN	A	131	12.244	4.033	29.259	1.00	11.04	8
ATOM	985	CB	ASN	A	131	12.331	1.939	31.372	1.00	9.40	6
ATOM	986	CG	ASN	A	131	11.721	2.692	32.537	1.00	9.88	6
ATOM	987	OD1	ASN	A	131	10.903	2.118	33.269	1.00	10.13	8
ATOM	988	ND2	ASN	A	131	12.055	3.968	32.661	1.00	9.63	7
ATOM	989	N	LEU	A	132	9.984	3.975	29.880	1.00	8.49	7
ATOM	990	CA	LEU	A	132	9.726	5.379	29.557	1.00	9.46	6
ATOM	991	C	LEU	A	132	9.192	6.133	30.788	1.00	9.52	6
ATOM	992	O	LEU	A	132	8.007	6.230	31.045	1.00	9.42	8
ATOM	993	CB	LEU	A	132	8.612	5.453	28.466	1.00	9.79	6
ATOM	994	CG	LEU	A	132	9.154	4.944	27.085	1.00	11.13	6
ATOM	995	CD1	LEU	A	132	8.014	4.418	26.261	1.00	12.43	6
ATOM	996	CD2	LEU	A	132	9.822	6.117	26.408	1.00	15.07	6
ATOM	997	N	SER	A	133	10.203	6.676	31.523	1.00	9.31	7
ATOM	998	CA	SER	A	133	9.908	7.485	32.708	1.00	8.09	6
ATOM	999	C	SER	A	133	9.697	8.938	32.219	1.00	9.51	6
ATOM	1000	O	SER	A	133	10.434	9.828	32.570	1.00	12.68	8
ATOM	1001	CB	SER	A	133	11.008	7.383	33.752	1.00	10.34	6
ATOM	1002	OG	SER	A	133	10.943	6.119	34.401	1.00	9.84	8
ATOM	1003	N	LEU	A	134	8.623	9.104	31.429	1.00	9.63	7
ATOM	1004	CA	LEU	A	134	8.400	10.415	30.762	1.00	9.62	6
ATOM	1005	C	LEU	A	134	6.942	10.351	30.296	1.00	12.30	6
ATOM	1006	O	LEU	A	134	6.298	9.299	30.147	1.00	11.68	8
ATOM	1007	CB	LEU	A	134	9.378	10.676	29.612	1.00	12.20	6
ATOM	1008	CG	LEU	A	134	9.390	9.650	28.500	1.00	11.16	6
ATOM	1009	CD1	LEU	A	134	8.275	9.976	27.482	1.00	13.93	6

ATOM	1010	CD2	LEU	A	134	10.722	9.590	27.782	1.00	16.32	6
ATOM	1011	N	GLY	A	135	6.429	11.549	29.949	1.00	12.94	7
ATOM	1012	CA	GLY	A	135	5.066	11.531	29.372	1.00	16.25	6
ATOM	1013	C	GLY	A	135	4.494	12.937	29.388	1.00	20.76	6
ATOM	1014	O	GLY	A	135	5.104	13.911	29.837	1.00	19.61	8
ATOM	1015	N	CYS	A	136	3.264	12.934	28.855	1.00	16.71	7
ATOM	1016	CA	CYS	A	136	2.541	14.220	28.850	1.00	20.54	6
ATOM	1017	C	CYS	A	136	1.077	13.966	28.524	1.00	16.55	6
ATOM	1018	O	CYS	A	136	0.649	12.886	28.170	1.00	14.70	8
ATOM	1019	CB	CYS	A	136	3.085	15.195	27.836	1.00	22.72	6
ATOM	1020	SG	CYS	A	136	3.714	14.546	26.303	1.00	26.03	16
ATOM	1021	N	GLU	A	137	0.333	15.093	28.682	1.00	18.30	7
ATOM	1022	CA	GLU	A	137	-1.056	15.040	28.175	1.00	17.88	6
ATOM	1023	C	GLU	A	137	-1.003	15.557	26.748	1.00	22.52	6
ATOM	1024	O	GLU	A	137	-1.289	16.704	26.391	1.00	21.83	8
ATOM	1025	CB	GLU	A	137	-2.021	15.837	29.031	1.00	20.26	6
ATOM	1026	CG	GLU	A	137	-2.281	15.296	30.439	1.00	22.38	6
ATOM	1027	CD	GLU	A	137	-3.418	16.130	31.064	1.00	26.72	6
ATOM	1028	OE1	GLU	A	137	-3.051	17.088	31.746	1.00	35.28	8
ATOM	1029	OE2	GLU	A	137	-4.576	15.757	30.819	1.00	21.07	8
ATOM	1030	N	CYS	A	138	-0.616	14.673	25.866	1.00	21.75	7
ATOM	1031	CA	CYS	A	138	-0.209	14.969	24.515	1.00	27.45	6
ATOM	1032	C	CYS	A	138	-0.666	13.873	23.581	1.00	31.92	6
ATOM	1033	O	CYS	A	138	-0.656	12.705	23.982	1.00	30.57	8
ATOM	1034	CB	CYS	A	138	1.332	15.100	24.522	1.00	29.63	6
ATOM	1035	SG	CYS	A	138	2.180	13.664	25.316	1.00	26.98	16
ATOM	1036	N	ASN	A	139	-1.166	14.258	22.421	1.00	30.94	7
ATOM	1037	CA	ASN	A	139	-1.597	13.300	21.407	1.00	30.40	6
ATOM	1038	C	ASN	A	139	-0.544	13.308	20.306	1.00	27.83	6
ATOM	1039	O	ASN	A	139	-0.056	14.362	19.882	1.00	27.73	8
ATOM	1040	CB	ASN	A	139	-2.957	13.676	20.845	1.00	34.15	6
ATOM	1041	CG	ASN	A	139	-4.122	12.993	21.530	1.00	44.83	6
ATOM	1042	OD1	ASN	A	139	-4.207	13.025	22.756	1.00	38.38	8
ATOM	1043	ND2	ASN	A	139	-4.999	12.389	20.735	1.00	50.90	7
ATOM	1044	N	SER	A	140	-0.166	12.120	19.829	1.00	18.15	7
ATOM	1045	CA	SER	A	140	0.870	12.081	18.795	1.00	18.59	6
ATOM	1046	C	SER	A	140	0.759	10.738	18.087	1.00	16.05	6
ATOM	1047	O	SER	A	140	0.941	9.697	18.736	1.00	16.64	8
ATOM	1048	CB	SER	A	140	2.267	12.165	19.402	1.00	20.72	6
ATOM	1049	OG	SER	A	140	3.309	11.908	18.514	1.00	23.30	8
ATOM	1050	N	THR	A	141	0.370	10.712	16.804	1.00	18.63	7
ATOM	1051	CA	THR	A	141	0.271	9.420	16.137	1.00	18.09	6
ATOM	1052	C	THR	A	141	1.670	8.843	15.884	1.00	15.35	6
ATOM	1053	O	THR	A	141	1.750	7.578	15.886	1.00	15.18	8
ATOM	1054	CB	THR	A	141	-0.540	9.429	14.838	1.00	20.90	6
ATOM	1055	OG1	THR	A	141	0.118	10.358	13.966	1.00	23.57	8
ATOM	1056	CG2	THR	A	141	-1.990	9.800	15.085	1.00	17.57	6
ATOM	1057	N	THR	A	142	2.720	9.626	15.861	1.00	16.63	7
ATOM	1058	CA	THR	A	142	4.094	9.149	15.775	1.00	14.88	6
ATOM	1059	C	THR	A	142	4.529	8.429	17.053	1.00	13.11	6
ATOM	1060	O	THR	A	142	5.094	7.345	16.979	1.00	14.05	8
ATOM	1061	CB	THR	A	142	4.997	10.341	15.457	1.00	24.16	6
ATOM	1062	OG1	THR	A	142	4.523	10.835	14.153	1.00	28.29	8
ATOM	1063	CG2	THR	A	142	6.432	9.970	15.210	1.00	26.14	6
ATOM	1064	N	LEU	A	143	4.124	8.997	18.199	1.00	13.69	7
ATOM	1065	CA	LEU	A	143	4.512	8.335	19.463	1.00	13.71	6
ATOM	1066	C	LEU	A	143	3.729	7.043	19.617	1.00	12.67	6
ATOM	1067	O	LEU	A	143	4.267	6.012	20.055	1.00	11.28	8
ATOM	1068	CB	LEU	A	143	4.184	9.316	20.618	1.00	12.30	6
ATOM	1069	CG	LEU	A	143	4.738	8.845	21.995	1.00	15.95	6
ATOM	1070	CD1	LEU	A	143	6.227	8.878	22.029	1.00	15.41	6
ATOM	1071	CD2	LEU	A	143	4.099	9.884	22.948	1.00	15.72	6
ATOM	1072	N	LYS	A	144	2.400	7.101	19.314	1.00	11.25	7
ATOM	1073	CA	LYS	A	144	1.651	5.858	19.420	1.00	11.23	6
ATOM	1074	C	LYS	A	144	2.211	4.764	18.517	1.00	10.18	6
ATOM	1075	O	LYS	A	144	2.312	3.600	18.899	1.00	10.89	8
ATOM	1076	CB	LYS	A	144	0.159	6.178	19.140	1.00	15.25	6
ATOM	1077	CG	LYS	A	144	-0.627	4.905	19.387	1.00	18.48	6

ATOM	1078	CD	LYS	A	144	-2.062	4.950	19.844	1.00	24.85	6
ATOM	1079	CE	LYS	A	144	-2.564	3.597	20.366	1.00	15.78	6
ATOM	1080	NZ	LYS	A	144	-2.599	2.616	19.228	1.00	14.78	7
ATOM	1081	N	SER	A	145	2.539	5.151	17.273	1.00	11.46	7
ATOM	1082	CA	SER	A	145	3.097	4.182	16.357	1.00	10.88	6
ATOM	1083	C	SER	A	145	4.407	3.579	16.834	1.00	10.64	6
ATOM	1084	O	SER	A	145	4.628	2.364	16.771	1.00	11.55	8
ATOM	1085	CB	SER	A	145	3.372	4.933	15.034	1.00	11.53	6
ATOM	1086	OG	SER	A	145	4.095	4.059	14.159	1.00	12.02	8
ATOM	1087	N	ALA	A	146	5.223	4.406	17.500	1.00	11.16	7
ATOM	1088	CA	ALA	A	146	6.521	3.907	17.961	1.00	10.64	6
ATOM	1089	C	ALA	A	146	6.280	2.864	19.071	1.00	8.68	6
ATOM	1090	O	ALA	A	146	6.945	1.842	19.103	1.00	10.24	8
ATOM	1091	CB	ALA	A	146	7.363	5.053	18.531	1.00	13.58	6
ATOM	1092	N	VAL	A	147	5.345	3.181	19.973	1.00	9.25	7
ATOM	1093	CA	VAL	A	147	5.063	2.216	21.057	1.00	10.47	6
ATOM	1094	C	VAL	A	147	4.479	0.936	20.530	1.00	9.13	6
ATOM	1095	O	VAL	A	147	4.842	-0.172	20.914	1.00	11.53	8
ATOM	1096	CB	VAL	A	147	4.051	2.840	22.072	1.00	9.11	6
ATOM	1097	CG1	VAL	A	147	3.468	1.828	23.057	1.00	10.14	6
ATOM	1098	CG2	VAL	A	147	4.741	3.918	22.848	1.00	11.38	6
ATOM	1099	N	ASP	A	148	3.531	1.044	19.538	1.00	10.88	7
ATOM	1100	CA	ASP	A	148	2.945	-0.158	18.998	1.00	9.20	6
ATOM	1101	C	ASP	A	148	3.904	-0.986	18.148	1.00	10.40	6
ATOM	1102	O	ASP	A	148	3.989	-2.216	18.235	1.00	12.08	8
ATOM	1103	CB	ASP	A	148	1.722	0.191	18.150	1.00	9.51	6
ATOM	1104	CG	ASP	A	148	0.523	0.649	18.916	1.00	12.65	6
ATOM	1105	OD1	ASP	A	148	-0.363	1.347	18.361	1.00	13.89	8
ATOM	1106	OD2	ASP	A	148	0.454	0.337	20.139	1.00	12.46	8
ATOM	1107	N	TYR	A	149	4.776	-0.203	17.443	1.00	10.28	7
ATOM	1108	CA	TYR	A	149	5.839	-0.920	16.701	1.00	11.03	6
ATOM	1109	C	TYR	A	149	6.725	-1.735	17.654	1.00	11.91	6
ATOM	1110	O	TYR	A	149	7.097	-2.870	17.371	1.00	11.38	8
ATOM	1111	CB	TYR	A	149	6.606	0.125	15.893	1.00	9.52	6
ATOM	1112	CG	TYR	A	149	7.854	-0.425	15.218	1.00	9.13	6
ATOM	1113	CD1	TYR	A	149	7.714	-1.156	14.034	1.00	13.04	6
ATOM	1114	CD2	TYR	A	149	9.133	-0.220	15.669	1.00	9.76	6
ATOM	1115	CE1	TYR	A	149	8.844	-1.655	13.380	1.00	11.71	6
ATOM	1116	CE2	TYR	A	149	10.277	-0.692	15.036	1.00	10.97	6
ATOM	1117	CZ	TYR	A	149	10.099	-1.415	13.843	1.00	13.29	6
ATOM	1118	OH	TYR	A	149	11.230	-1.879	13.246	1.00	12.70	8
ATOM	1119	N	ALA	A	150	7.149	-1.061	18.759	1.00	10.29	7
ATOM	1120	CA	ALA	A	150	8.086	-1.801	19.644	1.00	10.75	6
ATOM	1121	C	ALA	A	150	7.409	-3.014	20.263	1.00	12.48	6
ATOM	1122	O	ALA	A	150	7.986	-4.102	20.400	1.00	11.16	8
ATOM	1123	CB	ALA	A	150	8.414	-0.867	20.792	1.00	11.39	6
ATOM	1124	N	TRP	A	151	6.140	-2.882	20.642	1.00	9.91	7
ATOM	1125	CA	TRP	A	151	5.362	-4.015	21.124	1.00	10.13	6
ATOM	1126	C	TRP	A	151	5.261	-5.146	20.085	1.00	9.48	6
ATOM	1127	O	TRP	A	151	5.539	-6.305	20.358	1.00	10.95	8
ATOM	1128	CB	TRP	A	151	3.927	-3.582	21.579	1.00	10.48	6
ATOM	1129	CG	TRP	A	151	3.161	-4.785	21.971	1.00	11.85	6
ATOM	1130	CD1	TRP	A	151	2.277	-5.511	21.197	1.00	13.81	6
ATOM	1131	CD2	TRP	A	151	3.146	-5.490	23.235	1.00	9.96	6
ATOM	1132	NE1	TRP	A	151	1.771	-6.612	21.846	1.00	15.34	7
ATOM	1133	CE2	TRP	A	151	2.285	-6.592	23.111	1.00	11.52	6
ATOM	1134	CE3	TRP	A	151	3.799	-5.270	24.452	1.00	12.17	6
ATOM	1135	CZ2	TRP	A	151	2.055	-7.487	24.161	1.00	11.76	6
ATOM	1136	CZ3	TRP	A	151	3.603	-6.161	25.520	1.00	14.83	6
ATOM	1137	CH2	TRP	A	151	2.747	-7.235	25.354	1.00	11.91	6
ATOM	1138	N	ASN	A	152	4.921	-4.758	18.850	1.00	10.31	7
ATOM	1139	CA	ASN	A	152	4.758	-5.805	17.805	1.00	10.90	6
ATOM	1140	C	ASN	A	152	6.078	-6.365	17.381	1.00	12.51	6
ATOM	1141	O	ASN	A	152	6.094	-7.498	16.850	1.00	18.29	8
ATOM	1142	CB	ASN	A	152	4.057	-5.138	16.614	1.00	12.21	6
ATOM	1143	CG	ASN	A	152	2.596	-4.898	16.919	1.00	15.60	6
ATOM	1144	OD1	ASN	A	152	1.888	-5.697	17.581	1.00	16.16	8
ATOM	1145	ND2	ASN	A	152	2.084	-3.807	16.394	1.00	16.47	7

ATOM	1146	N	LYS	A	153	7.214	-5.769	17.698	1.00	12.60	7
ATOM	1147	CA	LYS	A	153	8.552	-6.282	17.497	1.00	12.34	6
ATOM	1148	C	LYS	A	153	8.890	-7.341	18.558	1.00	11.63	6
ATOM	1149	O	LYS	A	153	9.908	-8.014	18.454	1.00	16.70	8
ATOM	1150	CB	LYS	A	153	9.587	-5.158	17.537	1.00	14.85	6
ATOM	1151	CG	LYS	A	153	9.633	-4.265	16.316	1.00	21.79	6
ATOM	1152	CD	LYS	A	153	10.522	-4.776	15.210	1.00	20.60	6
ATOM	1153	CE	LYS	A	153	12.016	-4.864	15.642	1.00	14.64	6
ATOM	1154	NZ	LYS	A	153	12.600	-5.708	14.521	1.00	23.18	7
ATOM	1155	N	GLY	A	154	8.101	-7.351	19.658	1.00	11.47	7
ATOM	1156	CA	GLY	A	154	8.345	-8.288	20.722	1.00	10.77	6
ATOM	1157	C	GLY	A	154	8.817	-7.664	22.030	1.00	10.93	6
ATOM	1158	O	GLY	A	154	9.088	-8.468	22.922	1.00	12.36	8
ATOM	1159	N	ALA	A	155	8.909	-6.356	22.134	1.00	10.32	7
ATOM	1160	CA	ALA	A	155	9.381	-5.744	23.380	1.00	9.51	6
ATOM	1161	C	ALA	A	155	8.226	-5.469	24.340	1.00	10.33	6
ATOM	1162	O	ALA	A	155	7.074	-5.268	23.959	1.00	10.45	8
ATOM	1163	CB	ALA	A	155	10.101	-4.418	22.994	1.00	10.15	6
ATOM	1164	N	VAL	A	156	8.529	-5.419	25.626	1.00	10.20	7
ATOM	1165	CA	VAL	A	156	7.608	-4.930	26.644	1.00	9.64	6
ATOM	1166	C	VAL	A	156	7.900	-3.424	26.826	1.00	11.32	6
ATOM	1167	O	VAL	A	156	9.077	-3.071	26.918	1.00	11.90	8
ATOM	1168	CB	VAL	A	156	7.867	-5.665	27.974	1.00	8.78	6
ATOM	1169	CG1	VAL	A	156	6.965	-5.108	29.060	1.00	8.99	6
ATOM	1170	CG2	VAL	A	156	7.629	-7.139	27.784	1.00	10.63	6
ATOM	1171	N	VAL	A	157	6.818	-2.653	26.805	1.00	8.38	7
ATOM	1172	CA	VAL	A	157	6.923	-1.208	27.010	1.00	7.61	6
ATOM	1173	C	VAL	A	157	6.322	-0.872	28.402	1.00	7.95	6
ATOM	1174	O	VAL	A	157	5.156	-1.202	28.638	1.00	9.65	8
ATOM	1175	CB	VAL	A	157	6.194	-0.421	25.888	1.00	9.67	6
ATOM	1176	CG1	VAL	A	157	6.257	1.064	26.099	1.00	11.64	6
ATOM	1177	CG2	VAL	A	157	6.789	-0.831	24.528	1.00	11.35	6
ATOM	1178	N	VAL	A	158	7.116	-0.189	29.203	1.00	8.45	7
ATOM	1179	CA	VAL	A	158	6.700	0.190	30.574	1.00	9.13	6
ATOM	1180	C	VAL	A	158	6.807	1.706	30.663	1.00	9.56	6
ATOM	1181	O	VAL	A	158	7.873	2.222	30.248	1.00	9.44	8
ATOM	1182	CB	VAL	A	158	7.639	-0.489	31.598	1.00	8.39	6
ATOM	1183	CG1	VAL	A	158	7.139	-0.079	33.007	1.00	9.17	6
ATOM	1184	CG2	VAL	A	158	7.635	-2.003	31.414	1.00	9.94	6
ATOM	1185	N	ALA	A	159	5.799	2.385	31.165	1.00	8.36	7
ATOM	1186	CA	ALA	A	159	5.874	3.865	31.227	1.00	8.80	6
ATOM	1187	C	ALA	A	159	5.232	4.389	32.506	1.00	9.68	6
ATOM	1188	O	ALA	A	159	4.251	3.858	33.049	1.00	9.19	8
ATOM	1189	CB	ALA	A	159	5.122	4.442	30.023	1.00	11.81	6
ATOM	1190	N	ALA	A	160	5.842	5.486	32.979	1.00	10.16	7
ATOM	1191	CA	ALA	A	160	5.305	6.213	34.150	1.00	8.09	6
ATOM	1192	C	ALA	A	160	3.970	6.867	33.890	1.00	10.59	6
ATOM	1193	O	ALA	A	160	3.740	7.477	32.843	1.00	12.25	8
ATOM	1194	CB	ALA	A	160	6.379	7.244	34.509	1.00	10.91	6
ATOM	1195	N	ALA	A	161	3.077	6.756	34.901	1.00	10.18	7
ATOM	1196	CA	ALA	A	161	1.740	7.326	34.667	1.00	9.20	6
ATOM	1197	C	ALA	A	161	1.681	8.838	34.846	1.00	9.69	6
ATOM	1198	O	ALA	A	161	0.615	9.381	34.494	1.00	11.99	8
ATOM	1199	CB	ALA	A	161	0.757	6.678	35.666	1.00	11.17	6
ATOM	1200	N	GLY	A	162	2.697	9.461	35.379	1.00	10.16	7
ATOM	1201	CA	GLY	A	162	2.728	10.929	35.525	1.00	11.47	6
ATOM	1202	C	GLY	A	162	2.542	11.334	36.997	1.00	11.99	6
ATOM	1203	O	GLY	A	162	2.058	10.534	37.818	1.00	11.61	8
ATOM	1204	N	ASN	A	163	2.830	12.646	37.210	1.00	13.68	7
ATOM	1205	CA	ASN	A	163	3.016	13.100	38.616	1.00	14.00	6
ATOM	1206	C	ASN	A	163	2.233	14.384	38.911	1.00	14.39	6
ATOM	1207	O	ASN	A	163	2.725	15.174	39.760	1.00	18.79	8
ATOM	1208	CB	ASN	A	163	4.477	13.375	38.878	1.00	17.01	6
ATOM	1209	CG	ASN	A	163	5.442	12.263	38.552	1.00	20.97	6
ATOM	1210	OD1	ASN	A	163	5.223	11.120	38.907	1.00	22.23	8
ATOM	1211	ND2	ASN	A	163	6.522	12.569	37.843	1.00	40.92	7
ATOM	1212	N	ASP	A	164	1.039	14.444	38.394	1.00	14.22	7
ATOM	1213	CA	ASP	A	164	0.248	15.664	38.640	1.00	15.43	6

ATOM	1214	C	ASP	A	164	-0.891	15.376	39.610	1.00	16.52	6
ATOM	1215	O	ASP	A	164	-1.808	16.205	39.791	1.00	16.92	8
ATOM	1216	CB	ASP	A	164	-0.340	16.092	37.304	1.00	18.79	6
ATOM	1217	CG	ASP	A	164	0.611	16.817	36.382	1.00	31.26	6
ATOM	1218	OD1	ASP	A	164	0.099	17.435	35.437	1.00	32.77	8
ATOM	1219	OD2	ASP	A	164	1.843	16.799	36.578	1.00	32.99	8
ATOM	1220	N	ASN	A	165	-0.956	14.222	40.228	1.00	13.48	7
ATOM	1221	CA	ASN	A	165	-2.032	13.774	41.047	1.00	13.19	6
ATOM	1222	C	ASN	A	165	-3.417	13.950	40.424	1.00	12.14	6
ATOM	1223	O	ASN	A	165	-4.334	14.510	41.036	1.00	15.12	8
ATOM	1224	CB	ASN	A	165	-2.028	14.587	42.369	1.00	12.06	6
ATOM	1225	CG	ASN	A	165	-2.933	13.893	43.348	1.00	10.24	6
ATOM	1226	OD1	ASN	A	165	-3.244	12.729	43.479	1.00	12.45	8
ATOM	1227	ND2	ASN	A	165	-3.428	14.777	44.297	1.00	11.65	7
ATOM	1228	N	VAL	A	166	-3.533	13.571	39.169	1.00	12.64	7
ATOM	1229	CA	VAL	A	166	-4.803	13.600	38.442	1.00	13.30	6
ATOM	1230	C	VAL	A	166	-5.190	12.205	37.908	1.00	13.31	6
ATOM	1231	O	VAL	A	166	-4.366	11.280	37.855	1.00	11.72	8
ATOM	1232	CB	VAL	A	166	-4.852	14.651	37.330	1.00	15.75	6
ATOM	1233	CG1	VAL	A	166	-4.413	16.035	37.817	1.00	19.38	6
ATOM	1234	CG2	VAL	A	166	-3.879	14.327	36.205	1.00	15.73	6
ATOM	1235	N	SER	A	167	-6.430	12.097	37.425	1.00	15.05	7
ATOM	1236	CA	SER	A	167	-6.858	10.862	36.753	1.00	14.74	6
ATOM	1237	C	SER	A	167	-7.051	10.847	35.266	1.00	11.97	6
ATOM	1238	O	SER	A	167	-7.439	9.759	34.833	1.00	14.98	8
ATOM	1239	CB	SER	A	167	-8.159	10.374	37.453	1.00	21.93	6
ATOM	1240	OG	SER	A	167	-9.169	11.371	37.231	1.00	21.70	8
ATOM	1241	N	ARG	A	168	-6.733	12.019	34.760	1.00	14.80	7
ATOM	1242	CA	ARG	A	168	-6.628	12.185	33.336	1.00	14.30	6
ATOM	1243	C	ARG	A	168	-5.557	11.225	32.761	1.00	14.04	6
ATOM	1244	O	ARG	A	168	-4.583	11.016	33.472	1.00	16.56	8
ATOM	1245	CB	ARG	A	168	-6.450	13.600	32.868	1.00	14.72	6
ATOM	1246	CG	ARG	A	168	-7.590	14.492	33.412	1.00	17.52	6
ATOM	1247	CD	ARG	A	168	-7.488	15.866	32.744	1.00	19.22	6
ATOM	1248	NE	ARG	A	168	-6.152	16.434	32.854	1.00	19.87	7
ATOM	1249	CZ	ARG	A	168	-5.777	17.137	33.946	1.00	18.90	6
ATOM	1250	NH1	ARG	A	168	-6.683	17.234	34.915	1.00	22.35	7
ATOM	1251	NH2	ARG	A	168	-4.590	17.669	34.037	1.00	27.26	7
ATOM	1252	N	THR	A	169	-5.775	10.681	31.545	1.00	13.30	7
ATOM	1253	CA	THR	A	169	-4.663	9.851	31.036	1.00	14.18	6
ATOM	1254	C	THR	A	169	-3.476	10.689	30.653	1.00	14.82	6
ATOM	1255	O	THR	A	169	-3.422	11.859	30.220	1.00	16.21	8
ATOM	1256	CB	THR	A	169	-5.168	9.131	29.752	1.00	14.96	6
ATOM	1257	OG1	THR	A	169	-5.576	10.096	28.754	1.00	15.86	8
ATOM	1258	CG2	THR	A	169	-6.305	8.184	30.046	1.00	17.51	6
ATOM	1259	N	PHE	A	170	-2.290	10.036	30.708	1.00	12.69	7
ATOM	1260	CA	PHE	A	170	-0.978	10.559	30.350	1.00	10.15	6
ATOM	1261	C	PHE	A	170	-0.366	9.550	29.382	1.00	10.51	6
ATOM	1262	O	PHE	A	170	-0.516	8.340	29.517	1.00	13.04	8
ATOM	1263	CB	APHE	A	170	0.010	10.860	31.486	0.50	9.69	6
ATOM	1264	CG	APHE	A	170	-0.086	12.208	32.151	0.50	12.91	6
ATOM	1265	CD1	APHE	A	170	1.046	12.996	32.247	0.50	15.42	6
ATOM	1266	CD2	APHE	A	170	-1.271	12.657	32.723	0.50	15.96	6
ATOM	1267	CE1	APHE	A	170	0.999	14.230	32.893	0.50	17.60	6
ATOM	1268	CE2	APHE	A	170	-1.322	13.894	33.359	0.50	14.69	6
ATOM	1269	CZ	APHE	A	170	-0.193	14.664	33.434	0.50	18.78	6
ATOM	1270	CB	BPHE	A	170	-0.239	10.454	31.713	0.50	11.27	6
ATOM	1271	CG	BPHE	A	170	1.070	11.133	31.830	0.50	10.40	6
ATOM	1272	CD1	BPHE	A	170	2.277	10.418	31.853	0.50	10.22	6
ATOM	1273	CD2	BPHE	A	170	1.133	12.520	31.939	0.50	13.93	6
ATOM	1274	CE1	BPHE	A	170	3.482	11.075	31.968	0.50	12.32	6
ATOM	1275	CE2	BPHE	A	170	2.348	13.165	32.052	0.50	13.83	6
ATOM	1276	CZ	BPHE	A	170	3.544	12.456	32.077	0.50	15.52	6
ATOM	1277	N	GLN	A	171	0.238	10.113	28.331	1.00	11.14	7
ATOM	1278	CA	GLN	A	171	0.856	9.335	27.255	1.00	10.59	6
ATOM	1279	C	GLN	A	171	2.348	9.422	27.239	1.00	10.58	6
ATOM	1280	O	GLN	A	171	2.822	10.459	27.645	1.00	13.39	8
ATOM	1281	CB	GLN	A	171	0.297	9.849	25.865	1.00	11.19	6

ATOM	1282	CG	GLN	A	171	-1.200	9.613	25.647	1.00	11.83	6
ATOM	1283	CD	GLN	A	171	-2.121	10.468	26.524	1.00	13.12	6
ATOM	1284	OE1	GLN	A	171	-2.934	9.928	27.305	1.00	15.76	8
ATOM	1285	NE2	GLN	A	171	-2.011	11.790	26.391	1.00	14.42	7
ATOM	1286	N	PRO	A	172	3.043	8.320	26.919	1.00	11.03	7
ATOM	1287	CA	PRO	A	172	2.572	7.108	26.347	1.00	11.46	6
ATOM	1288	C	PRO	A	172	2.006	6.025	27.235	1.00	11.03	6
ATOM	1289	O	PRO	A	172	1.509	5.023	26.809	1.00	11.22	8
ATOM	1290	CB	PRO	A	172	3.819	6.511	25.610	1.00	11.89	6
ATOM	1291	CG	PRO	A	172	4.908	6.978	26.569	1.00	11.81	6
ATOM	1292	CD	PRO	A	172	4.490	8.404	26.935	1.00	12.12	6
ATOM	1293	N	ALA	A	173	2.069	6.254	28.594	1.00	9.12	7
ATOM	1294	CA	ALA	A	173	1.563	5.194	29.473	1.00	9.14	6
ATOM	1295	C	ALA	A	173	0.120	4.778	29.127	1.00	10.86	6
ATOM	1296	O	ALA	A	173	-0.157	3.582	29.296	1.00	11.28	8
ATOM	1297	CB	ALA	A	173	1.640	5.713	30.931	1.00	11.79	6
ATOM	1298	N	SER	A	174	-0.804	5.696	28.751	1.00	9.25	7
ATOM	1299	CA	SER	A	174	-2.184	5.257	28.562	1.00	10.77	6
ATOM	1300	C	SER	A	174	-2.434	4.456	27.262	1.00	11.85	6
ATOM	1301	O	SER	A	174	-3.559	3.938	27.120	1.00	12.90	8
ATOM	1302	CB	SER	A	174	-3.071	6.504	28.585	1.00	12.82	6
ATOM	1303	OG	SER	A	174	-2.887	7.251	27.376	1.00	13.72	8
ATOM	1304	N	TYR	A	175	-1.417	4.375	26.405	1.00	11.48	7
ATOM	1305	CA	TYR	A	175	-1.695	3.533	25.228	1.00	12.72	6
ATOM	1306	C	TYR	A	175	-1.927	2.094	25.655	1.00	10.63	6
ATOM	1307	O	TYR	A	175	-1.259	1.611	26.603	1.00	11.10	8
ATOM	1308	CB	TYR	A	175	-0.435	3.567	24.316	1.00	11.23	6
ATOM	1309	CG	TYR	A	175	-0.129	4.914	23.750	1.00	10.17	6
ATOM	1310	CD1	TYR	A	175	-1.068	5.887	23.517	1.00	13.17	6
ATOM	1311	CD2	TYR	A	175	1.198	5.229	23.425	1.00	9.64	6
ATOM	1312	CE1	TYR	A	175	-0.763	7.116	22.977	1.00	11.74	6
ATOM	1313	CE2	TYR	A	175	1.529	6.450	22.873	1.00	11.86	6
ATOM	1314	CZ	TYR	A	175	0.574	7.397	22.648	1.00	15.00	6
ATOM	1315	OH	TYR	A	175	0.880	8.636	22.122	1.00	16.46	8
ATOM	1316	N	PRO	A	176	-2.776	1.327	25.028	1.00	11.70	7
ATOM	1317	CA	PRO	A	176	-2.959	-0.092	25.360	1.00	11.01	6
ATOM	1318	C	PRO	A	176	-1.660	-0.878	25.468	1.00	10.13	6
ATOM	1319	O	PRO	A	176	-1.615	-1.766	26.289	1.00	11.27	8
ATOM	1320	CB	PRO	A	176	-3.990	-0.665	24.357	1.00	12.68	6
ATOM	1321	CG	PRO	A	176	-4.746	0.637	24.093	1.00	11.38	6
ATOM	1322	CD	PRO	A	176	-3.780	1.833	24.052	1.00	13.11	6
ATOM	1323	N	ASN	A	177	-0.723	-0.656	24.506	1.00	11.05	7
ATOM	1324	CA	ASN	A	177	0.441	-1.544	24.522	1.00	12.20	6
ATOM	1325	C	ASN	A	177	1.551	-1.045	25.410	1.00	11.24	6
ATOM	1326	O	ASN	A	177	2.629	-1.720	25.402	1.00	11.19	8
ATOM	1327	CB	ASN	A	177	0.857	-1.640	23.046	1.00	10.48	6
ATOM	1328	CG	ASN	A	177	0.051	-2.684	22.321	1.00	12.91	6
ATOM	1329	OD1	ASN	A	177	-0.414	-3.689	22.832	1.00	14.78	8
ATOM	1330	ND2	ASN	A	177	-0.019	-2.441	20.970	1.00	15.54	7
ATOM	1331	N	ALA	A	178	1.283	-0.058	26.278	1.00	10.52	7
ATOM	1332	CA	ALA	A	178	2.264	0.293	27.312	1.00	9.20	6
ATOM	1333	C	ALA	A	178	1.728	-0.191	28.662	1.00	11.35	6
ATOM	1334	O	ALA	A	178	0.548	0.004	28.907	1.00	10.58	8
ATOM	1335	CB	ALA	A	178	2.471	1.825	27.370	1.00	11.60	6
ATOM	1336	N	ILE	A	179	2.559	-0.779	29.554	1.00	9.76	7
ATOM	1337	CA	ILE	A	179	2.080	-0.944	30.966	1.00	8.57	6
ATOM	1338	C	ILE	A	179	2.217	0.427	31.641	1.00	9.10	6
ATOM	1339	O	ILE	A	179	3.315	0.926	31.750	1.00	10.06	8
ATOM	1340	CB	ILE	A	179	3.011	-1.961	31.637	1.00	8.69	6
ATOM	1341	CG1	ILE	A	179	2.926	-3.292	30.879	1.00	11.26	6
ATOM	1342	CG2	ILE	A	179	2.632	-2.226	33.097	1.00	10.57	6
ATOM	1343	CD1	ILE	A	179	3.905	-4.323	31.403	1.00	13.43	6
ATOM	1344	N	ALA	A	180	1.097	0.950	32.181	1.00	8.93	7
ATOM	1345	CA	ALA	A	180	1.104	2.243	32.870	1.00	8.88	6
ATOM	1346	C	ALA	A	180	1.312	1.988	34.378	1.00	9.81	6
ATOM	1347	O	ALA	A	180	0.623	1.134	34.956	1.00	10.08	8
ATOM	1348	CB	ALA	A	180	-0.257	2.936	32.657	1.00	10.99	6
ATOM	1349	N	VAL	A	181	2.333	2.692	34.886	1.00	8.81	7

ATOM	1350	CA	VAL	A	181	2.750	2.473	36.298	1.00	7.21	6
ATOM	1351	C	VAL	A	181	2.625	3.698	37.175	1.00	10.43	6
ATOM	1352	O	VAL	A	181	3.187	4.746	36.896	1.00	9.18	8
ATOM	1353	CB	VAL	A	181	4.252	2.124	36.222	1.00	7.41	6
ATOM	1354	CG1	VAL	A	181	4.729	1.806	37.634	1.00	9.89	6
ATOM	1355	CG2	VAL	A	181	4.527	0.886	35.362	1.00	8.70	6
ATOM	1356	N	GLY	A	182	1.839	3.465	38.248	1.00	10.46	7
ATOM	1357	CA	GLY	A	182	1.639	4.475	39.285	1.00	9.36	6
ATOM	1358	C	GLY	A	182	2.682	4.200	40.403	1.00	10.52	6
ATOM	1359	O	GLY	A	182	3.453	3.263	40.320	1.00	10.35	8
ATOM	1360	N	ALA	A	183	2.714	5.147	41.349	1.00	9.62	7
ATOM	1361	CA	ALA	A	183	3.677	4.975	42.430	1.00	8.49	6
ATOM	1362	C	ALA	A	183	2.990	4.939	43.792	1.00	10.18	6
ATOM	1363	O	ALA	A	183	2.028	5.635	44.041	1.00	10.96	8
ATOM	1364	CB	ALA	A	183	4.536	6.262	42.471	1.00	11.75	6
ATOM	1365	N	ILE	A	184	3.671	4.126	44.619	1.00	8.08	7
ATOM	1366	CA	ILE	A	184	3.277	4.029	46.044	1.00	9.34	6
ATOM	1367	C	ILE	A	184	4.522	4.315	46.889	1.00	10.84	6
ATOM	1368	O	ILE	A	184	5.660	4.279	46.425	1.00	10.59	8
ATOM	1369	CB	ILE	A	184	2.765	2.623	46.440	1.00	9.26	6
ATOM	1370	CG1	ILE	A	184	3.623	1.537	45.777	1.00	9.29	6
ATOM	1371	CG2	ILE	A	184	1.298	2.458	46.049	1.00	10.38	6
ATOM	1372	CD1	ILE	A	184	3.337	0.145	46.343	1.00	9.89	6
ATOM	1373	N	ASP	A	185	4.246	4.604	48.177	1.00	9.31	7
ATOM	1374	CA	ASP	A	185	5.388	4.755	49.122	1.00	11.76	6
ATOM	1375	C	ASP	A	185	5.646	3.419	49.776	1.00	9.50	6
ATOM	1376	O	ASP	A	185	5.128	2.363	49.400	1.00	11.06	8
ATOM	1377	CB	ASP	A	185	4.996	5.878	50.077	1.00	12.42	6
ATOM	1378	CG	ASP	A	185	3.878	5.520	51.008	1.00	16.62	6
ATOM	1379	OD1	ASP	A	185	3.498	4.359	51.188	1.00	19.16	8
ATOM	1380	OD2	ASP	A	185	3.331	6.525	51.584	1.00	21.71	8
ATOM	1381	N	SER	A	186	6.557	3.525	50.791	1.00	10.02	7
ATOM	1382	CA	SER	A	186	6.943	2.275	51.483	1.00	11.07	6
ATOM	1383	C	SER	A	186	5.904	1.628	52.388	1.00	11.68	6
ATOM	1384	O	SER	A	186	6.089	0.458	52.791	1.00	12.40	8
ATOM	1385	CB	SER	A	186	8.278	2.475	52.195	1.00	12.70	6
ATOM	1386	OG	SER	A	186	8.020	3.342	53.353	1.00	13.04	8
ATOM	1387	N	ASN	A	187	4.805	2.372	52.571	1.00	12.58	7
ATOM	1388	CA	ASN	A	187	3.674	1.829	53.284	1.00	11.75	6
ATOM	1389	C	ASN	A	187	2.521	1.414	52.403	1.00	14.42	6
ATOM	1390	O	ASN	A	187	1.387	1.286	52.844	1.00	14.41	8
ATOM	1391	CB	ASN	A	187	3.208	2.885	54.299	1.00	13.43	6
ATOM	1392	CG	ASN	A	187	2.435	2.266	55.455	1.00	24.32	6
ATOM	1393	OD1	ASN	A	187	2.664	1.109	55.787	1.00	28.21	8
ATOM	1394	ND2	ASN	A	187	1.561	3.083	56.015	1.00	24.99	7
ATOM	1395	N	ASP	A	188	2.816	1.287	51.095	1.00	12.93	7
ATOM	1396	CA	ASP	A	188	1.790	0.919	50.135	1.00	12.49	6
ATOM	1397	C	ASP	A	188	0.681	1.950	49.920	1.00	12.89	6
ATOM	1398	O	ASP	A	188	-0.362	1.549	49.382	1.00	16.50	8
ATOM	1399	CB	ASP	A	188	1.210	-0.478	50.410	1.00	14.69	6
ATOM	1400	CG	ASP	A	188	2.107	-1.661	50.168	1.00	14.67	6
ATOM	1401	OD1	ASP	A	188	3.257	-1.503	49.644	1.00	15.16	8
ATOM	1402	OD2	ASP	A	188	1.754	-2.821	50.535	1.00	17.10	8
ATOM	1403	N	ARG	A	189	0.944	3.168	50.317	1.00	11.91	7
ATOM	1404	CA	ARG	A	189	-0.057	4.193	50.068	1.00	11.81	6
ATOM	1405	C	ARG	A	189	0.318	4.940	48.809	1.00	10.44	6
ATOM	1406	O	ARG	A	189	1.490	5.032	48.450	1.00	11.22	8
ATOM	1407	CB	ARG	A	189	-0.070	5.188	51.257	1.00	12.95	6
ATOM	1408	CG	ARG	A	189	-0.635	4.385	52.458	1.00	19.11	6
ATOM	1409	CD	ARG	A	189	-0.942	5.273	53.602	0.00	20.00	6
ATOM	1410	NE	ARG	A	189	-1.563	4.465	54.658	0.00	20.00	7
ATOM	1411	CZ	ARG	A	189	-2.073	5.120	55.718	0.00	20.00	6
ATOM	1412	NH1	ARG	A	189	-2.009	6.439	55.778	0.00	20.00	7
ATOM	1413	NH2	ARG	A	189	-2.641	4.429	56.712	0.00	20.00	7
ATOM	1414	N	LYS	A	190	-0.725	5.371	48.044	1.00	12.65	7
ATOM	1415	CA	LYS	A	190	-0.437	6.168	46.830	1.00	13.29	6
ATOM	1416	C	LYS	A	190	0.475	7.292	47.111	1.00	12.33	6
ATOM	1417	O	LYS	A	190	0.366	8.054	48.112	1.00	12.55	8

ATOM	1418	CB	LYS	A	190	-1.739	6.688	46.193	1.00	14.04	6
ATOM	1419	CG	LYS	A	190	-1.575	7.374	44.863	1.00	13.43	6
ATOM	1420	CD	LYS	A	190	-2.892	8.042	44.365	1.00	14.23	6
ATOM	1421	CE	LYS	A	190	-2.848	9.547	44.467	1.00	11.74	6
ATOM	1422	NZ	LYS	A	190	-1.794	10.509	44.344	1.00	14.74	7
ATOM	1423	N	ALA	A	191	1.539	7.488	46.284	1.00	9.54	7
ATOM	1424	CA	ALA	A	191	2.402	8.643	46.397	1.00	10.14	6
ATOM	1425	C	ALA	A	191	1.569	9.962	46.232	1.00	12.32	6
ATOM	1426	O	ALA	A	191	0.650	9.922	45.406	1.00	12.53	8
ATOM	1427	CB	ALA	A	191	3.479	8.638	45.324	1.00	12.15	6
ATOM	1428	N	SER	A	192	1.965	10.976	46.997	1.00	13.24	7
ATOM	1429	CA	SER	A	192	1.044	12.139	46.993	1.00	15.23	6
ATOM	1430	C	SER	A	192	0.868	12.637	45.580	1.00	11.65	6
ATOM	1431	O	SER	A	192	-0.259	13.044	45.208	1.00	11.90	8
ATOM	1432	CB	SER	A	192	1.586	13.158	48.008	1.00	19.44	6
ATOM	1433	OG	SER	A	192	2.765	13.652	47.508	1.00	23.70	8
ATOM	1434	N	PHE	A	193	1.863	12.658	44.721	1.00	12.20	7
ATOM	1435	CA	PHE	A	193	1.810	13.199	43.381	1.00	14.48	6
ATOM	1436	C	PHE	A	193	1.385	12.209	42.289	1.00	13.11	6
ATOM	1437	O	PHE	A	193	1.238	12.595	41.135	1.00	11.70	8
ATOM	1438	CB	PHE	A	193	3.310	13.582	43.106	1.00	17.86	6
ATOM	1439	CG	PHE	A	193	4.249	12.384	43.353	1.00	20.29	6
ATOM	1440	CD1	PHE	A	193	4.287	11.322	42.438	1.00	22.95	6
ATOM	1441	CD2	PHE	A	193	5.040	12.214	44.448	1.00	8.24	6
ATOM	1442	CE1	PHE	A	193	5.098	10.236	42.710	1.00	19.68	6
ATOM	1443	CE2	PHE	A	193	5.864	11.222	44.781	1.00	21.76	6
ATOM	1444	CZ	PHE	A	193	5.910	10.164	43.860	1.00	19.49	6
ATOM	1445	N	SER	A	194	1.240	10.942	42.667	1.00	10.08	7
ATOM	1446	CA	SER	A	194	1.056	10.001	41.524	1.00	9.55	6
ATOM	1447	C	SER	A	194	-0.269	10.206	40.817	1.00	10.73	6
ATOM	1448	O	SER	A	194	-1.304	10.320	41.445	1.00	11.77	8
ATOM	1449	CB	SER	A	194	1.096	8.580	42.077	1.00	10.02	6
ATOM	1450	OG	SER	A	194	0.951	7.609	41.021	1.00	11.46	8
ATOM	1451	N	ASN	A	195	-0.250	10.146	39.487	1.00	9.56	7
ATOM	1452	CA	ASN	A	195	-1.500	10.042	38.765	1.00	9.33	6
ATOM	1453	C	ASN	A	195	-2.095	8.658	39.068	1.00	12.48	6
ATOM	1454	O	ASN	A	195	-1.471	7.723	39.599	1.00	11.95	8
ATOM	1455	CB	ASN	A	195	-1.288	10.176	37.252	1.00	9.08	6
ATOM	1456	CG	ASN	A	195	-0.941	11.572	36.865	1.00	11.88	6
ATOM	1457	OD1	ASN	A	195	-1.104	12.515	37.608	1.00	12.04	8
ATOM	1458	ND2	ASN	A	195	-0.437	11.729	35.635	1.00	12.30	7
ATOM	1459	N	TYR	A	196	-3.396	8.535	38.769	1.00	11.14	7
ATOM	1460	CA	TYR	A	196	-4.117	7.344	39.186	1.00	9.82	6
ATOM	1461	C	TYR	A	196	-5.386	7.196	38.350	1.00	13.03	6
ATOM	1462	O	TYR	A	196	-5.716	8.132	37.629	1.00	14.68	8
ATOM	1463	CB	TYR	A	196	-4.544	7.490	40.681	1.00	11.85	6
ATOM	1464	CG	TYR	A	196	-5.414	8.701	40.933	1.00	12.37	6
ATOM	1465	CD1	TYR	A	196	-4.871	9.945	41.165	1.00	12.29	6
ATOM	1466	CD2	TYR	A	196	-6.802	8.592	40.906	1.00	11.59	6
ATOM	1467	CE1	TYR	A	196	-5.612	11.084	41.371	1.00	13.98	6
ATOM	1468	CE2	TYR	A	196	-7.586	9.704	41.112	1.00	15.81	6
ATOM	1469	CZ	TYR	A	196	-7.009	10.918	41.336	1.00	15.20	6
ATOM	1470	OH	TYR	A	196	-7.817	12.040	41.542	1.00	19.65	8
ATOM	1471	N	GLY	A	197	-5.882	5.993	38.403	1.00	11.13	7
ATOM	1472	CA	GLY	A	197	-7.170	5.755	37.680	1.00	11.68	6
ATOM	1473	C	GLY	A	197	-7.164	4.338	37.161	1.00	12.24	6
ATOM	1474	O	GLY	A	197	-6.200	3.578	37.267	1.00	13.15	8
ATOM	1475	N	THR	A	198	-8.311	3.905	36.542	1.00	12.40	7
ATOM	1476	CA	THR	A	198	-8.425	2.531	36.111	1.00	11.46	6
ATOM	1477	C	THR	A	198	-7.578	2.248	34.855	1.00	12.92	6
ATOM	1478	O	THR	A	198	-7.329	1.063	34.613	1.00	14.81	8
ATOM	1479	CB	THR	A	198	-9.918	2.151	35.818	1.00	13.71	6
ATOM	1480	OG1	THR	A	198	-10.361	2.988	34.785	1.00	20.98	8
ATOM	1481	CG2	THR	A	198	-10.785	2.300	37.056	1.00	17.57	6
ATOM	1482	N	TRP	A	199	-7.107	3.325	34.195	1.00	12.12	7
ATOM	1483	CA	TRP	A	199	-6.192	3.157	33.081	1.00	12.81	6
ATOM	1484	C	TRP	A	199	-4.774	2.869	33.525	1.00	11.15	6
ATOM	1485	O	TRP	A	199	-3.896	2.557	32.737	1.00	13.41	8

ATOM	1486	CB	TRP	A	199	-6.194	4.421	32.173	1.00	11.96	6
ATOM	1487	CG	TRP	A	199	-5.744	5.662	32.884	1.00	11.22	6
ATOM	1488	CD1	TRP	A	199	-6.470	6.564	33.633	1.00	16.14	6
ATOM	1489	CD2	TRP	A	199	-4.419	6.188	32.931	1.00	10.56	6
ATOM	1490	NE1	TRP	A	199	-5.702	7.565	34.144	1.00	16.05	7
ATOM	1491	CE2	TRP	A	199	-4.397	7.379	33.705	1.00	14.41	6
ATOM	1492	CE3	TRP	A	199	-3.218	5.745	32.325	1.00	12.64	6
ATOM	1493	CZ2	TRP	A	199	-3.239	8.128	33.914	1.00	17.36	6
ATOM	1494	CZ3	TRP	A	199	-2.092	6.505	32.566	1.00	15.03	6
ATOM	1495	CH2	TRP	A	199	-2.081	7.654	33.347	1.00	14.87	6
ATOM	1496	N	VAL	A	200	-4.468	3.143	34.811	1.00	10.34	7
ATOM	1497	CA	VAL	A	200	-3.115	2.805	35.303	1.00	12.70	6
ATOM	1498	C	VAL	A	200	-3.087	1.330	35.623	1.00	11.86	6
ATOM	1499	O	VAL	A	200	-4.069	0.763	36.157	1.00	14.02	8
ATOM	1500	CB	VAL	A	200	-2.815	3.607	36.568	1.00	10.90	6
ATOM	1501	CG1	VAL	A	200	-1.476	3.218	37.118	1.00	11.75	6
ATOM	1502	CG2	VAL	A	200	-2.907	5.097	36.300	1.00	10.81	6
ATOM	1503	N	ASP	A	201	-2.127	0.525	35.152	1.00	9.45	7
ATOM	1504	CA	ASP	A	201	-2.205	-0.917	35.269	1.00	10.79	6
ATOM	1505	C	ASP	A	201	-1.714	-1.428	36.611	1.00	11.73	6
ATOM	1506	O	ASP	A	201	-2.428	-2.193	37.259	1.00	10.74	8
ATOM	1507	CB	ASP	A	201	-1.361	-1.532	34.104	1.00	10.60	6
ATOM	1508	CG	ASP	A	201	-2.014	-1.237	32.785	1.00	14.68	6
ATOM	1509	OD1	ASP	A	201	-3.197	-1.603	32.591	1.00	12.39	8
ATOM	1510	OD2	ASP	A	201	-1.329	-0.642	31.929	1.00	11.24	8
ATOM	1511	N	VAL	A	202	-0.478	-1.016	36.955	1.00	10.17	7
ATOM	1512	CA	VAL	A	202	0.069	-1.498	38.207	1.00	10.76	6
ATOM	1513	C	VAL	A	202	0.716	-0.337	38.925	1.00	9.89	6
ATOM	1514	O	VAL	A	202	0.872	0.733	38.352	1.00	9.72	8
ATOM	1515	CB	VAL	A	202	1.128	-2.591	38.016	1.00	9.97	6
ATOM	1516	CG1	VAL	A	202	0.504	-3.847	37.440	1.00	12.13	6
ATOM	1517	CG2	VAL	A	202	2.283	-2.104	37.130	1.00	14.06	6
ATOM	1518	N	THR	A	203	1.041	-0.552	40.192	1.00	9.69	7
ATOM	1519	CA	THR	A	203	1.817	0.426	40.984	1.00	8.33	6
ATOM	1520	C	THR	A	203	3.076	-0.208	41.542	1.00	8.20	6
ATOM	1521	O	THR	A	203	3.152	-1.455	41.659	1.00	8.89	8
ATOM	1522	CB	THR	A	203	0.899	1.018	42.077	1.00	10.11	6
ATOM	1523	OG1	THR	A	203	1.528	2.183	42.573	1.00	9.97	8
ATOM	1524	CG2	THR	A	203	0.604	0.003	43.200	1.00	10.55	6
ATOM	1525	N	ALA	A	204	4.060	0.625	41.900	1.00	8.43	7
ATOM	1526	CA	ALA	A	204	5.322	0.114	42.440	1.00	7.80	6
ATOM	1527	C	ALA	A	204	5.934	1.201	43.307	1.00	7.92	6
ATOM	1528	O	ALA	A	204	5.639	2.403	43.176	1.00	8.87	8
ATOM	1529	CB	ALA	A	204	6.215	-0.218	41.206	1.00	9.02	6
ATOM	1530	N	PRO	A	205	6.889	0.857	44.167	1.00	9.20	7
ATOM	1531	CA	PRO	A	205	7.626	1.788	44.988	1.00	10.66	6
ATOM	1532	C	PRO	A	205	8.167	2.923	44.122	1.00	10.80	6
ATOM	1533	O	PRO	A	205	8.865	2.755	43.103	1.00	10.53	8
ATOM	1534	CB	PRO	A	205	8.810	0.934	45.486	1.00	11.87	6
ATOM	1535	CG	PRO	A	205	8.066	-0.386	45.743	1.00	9.61	6
ATOM	1536	CD	PRO	A	205	7.222	-0.568	44.424	1.00	10.97	6
ATOM	1537	N	GLY	A	206	7.855	4.139	44.552	1.00	9.51	7
ATOM	1538	CA	GLY	A	206	8.265	5.328	43.848	1.00	8.77	6
ATOM	1539	C	GLY	A	206	8.571	6.543	44.702	1.00	9.82	6
ATOM	1540	O	GLY	A	206	8.762	7.640	44.198	1.00	12.47	8
ATOM	1541	N	VAL	A	207	8.608	6.363	46.053	1.00	9.75	7
ATOM	1542	CA	VAL	A	207	8.789	7.498	46.954	1.00	11.01	6
ATOM	1543	C	VAL	A	207	10.120	7.353	47.646	1.00	10.23	6
ATOM	1544	O	VAL	A	207	10.366	6.348	48.257	1.00	11.51	8
ATOM	1545	CB	VAL	A	207	7.679	7.624	48.011	1.00	9.92	6
ATOM	1546	CG1	VAL	A	207	7.938	8.802	48.933	1.00	10.74	6
ATOM	1547	CG2	VAL	A	207	6.369	7.832	47.256	1.00	12.64	6
ATOM	1548	N	ASN	A	208	10.960	8.360	47.573	1.00	9.70	7
ATOM	1549	CA	ASN	A	208	12.257	8.317	48.278	1.00	9.99	6
ATOM	1550	C	ASN	A	208	13.030	7.058	47.981	1.00	9.86	6
ATOM	1551	O	ASN	A	208	13.447	6.265	48.772	1.00	10.57	8
ATOM	1552	CB	ASN	A	208	12.033	8.481	49.791	1.00	12.47	6
ATOM	1553	CG	ASN	A	208	11.614	9.893	50.142	1.00	16.00	6

ATOM	1554	OD1	ASN	A	208	11.947	10.841	49.487	1.00	17.81	8
ATOM	1555	ND2	ASN	A	208	10.820	9.952	51.225	1.00	23.41	7
ATOM	1556	N	ILE	A	209	13.185	6.904	46.648	1.00	11.72	7
ATOM	1557	CA	ILE	A	209	13.934	5.767	46.091	1.00	11.01	6
ATOM	1558	C	ILE	A	209	15.425	6.097	45.962	1.00	10.83	6
ATOM	1559	O	ILE	A	209	15.707	7.084	45.253	1.00	10.52	8
ATOM	1560	CB	ILE	A	209	13.406	5.365	44.711	1.00	9.48	6
ATOM	1561	CG1	ILE	A	209	11.918	4.982	44.806	1.00	9.44	6
ATOM	1562	CG2	ILE	A	209	14.242	4.273	44.034	1.00	10.15	6
ATOM	1563	CD1	ILE	A	209	11.642	3.820	45.762	1.00	9.01	6
ATOM	1564	N	ALA	A	210	16.292	5.399	46.705	1.00	8.36	7
ATOM	1565	CA	ALA	A	210	17.741	5.665	46.491	1.00	9.20	6
ATOM	1566	C	ALA	A	210	18.266	5.060	45.191	1.00	11.06	6
ATOM	1567	O	ALA	A	210	18.035	3.879	45.016	1.00	11.02	8
ATOM	1568	CB	ALA	A	210	18.464	5.038	47.678	1.00	10.57	6
ATOM	1569	N	SER	A	211	19.037	5.807	44.408	1.00	10.47	7
ATOM	1570	CA	SER	A	211	19.647	5.229	43.209	1.00	9.26	6
ATOM	1571	C	SER	A	211	20.849	6.075	42.839	1.00	10.82	6
ATOM	1572	O	SER	A	211	21.241	7.011	43.573	1.00	12.70	8
ATOM	1573	CB	SER	A	211	18.572	5.218	42.076	1.00	11.65	6
ATOM	1574	OG	SER	A	211	19.186	4.429	41.031	1.00	9.57	8
ATOM	1575	N	THR	A	212	21.521	5.684	41.776	1.00	9.45	7
ATOM	1576	CA	THR	A	212	22.650	6.435	41.237	1.00	9.57	6
ATOM	1577	C	THR	A	212	22.316	7.786	40.601	1.00	10.33	6
ATOM	1578	O	THR	A	212	21.312	7.897	39.943	1.00	11.17	8
ATOM	1579	CB	THR	A	212	23.230	5.539	40.123	1.00	10.82	6
ATOM	1580	OG1	THR	A	212	22.197	5.032	39.255	1.00	11.01	8
ATOM	1581	CG2	THR	A	212	23.860	4.247	40.683	1.00	11.54	6
ATOM	1582	N	VAL	A	213	23.202	8.751	40.854	1.00	11.50	7
ATOM	1583	CA	VAL	A	213	23.084	10.032	40.112	1.00	10.64	6
ATOM	1584	C	VAL	A	213	24.479	10.365	39.618	1.00	12.70	6
ATOM	1585	O	VAL	A	213	25.449	9.733	40.023	1.00	14.01	8
ATOM	1586	CB	VAL	A	213	22.430	11.117	40.929	1.00	10.58	6
ATOM	1587	CG1	VAL	A	213	20.952	10.866	41.236	1.00	15.95	6
ATOM	1588	CG2	VAL	A	213	23.176	11.444	42.212	1.00	16.49	6
ATOM	1589	N	PRO	A	214	24.599	11.271	38.634	1.00	12.29	7
ATOM	1590	CA	PRO	A	214	25.893	11.455	38.032	1.00	14.14	6
ATOM	1591	C	PRO	A	214	27.016	11.909	38.959	1.00	15.71	6
ATOM	1592	O	PRO	A	214	26.744	12.410	40.052	1.00	16.38	8
ATOM	1593	CB	PRO	A	214	25.641	12.502	36.919	1.00	15.16	6
ATOM	1594	CG	PRO	A	214	24.175	12.119	36.585	1.00	11.84	6
ATOM	1595	CD	PRO	A	214	23.489	11.956	37.969	1.00	14.36	6
ATOM	1596	N	ASN	A	215	28.217	11.674	38.451	1.00	17.19	7
ATOM	1597	CA	ASN	A	215	29.421	12.081	39.228	1.00	19.26	6
ATOM	1598	C	ASN	A	215	29.493	11.275	40.514	1.00	18.85	6
ATOM	1599	O	ASN	A	215	29.781	11.814	41.595	1.00	21.66	8
ATOM	1600	CB	ASN	A	215	29.417	13.592	39.493	1.00	19.94	6
ATOM	1601	CG	ASN	A	215	29.256	14.419	38.223	1.00	31.85	6
ATOM	1602	OD1	ASN	A	215	29.976	14.179	37.251	1.00	28.69	8
ATOM	1603	ND2	ASN	A	215	28.346	15.396	38.116	1.00	31.00	7
ATOM	1604	N	ASN	A	216	29.395	9.955	40.364	1.00	15.65	7
ATOM	1605	CA	ASN	A	216	29.543	9.014	41.466	1.00	14.86	6
ATOM	1606	C	ASN	A	216	28.733	9.469	42.678	1.00	14.58	6
ATOM	1607	O	ASN	A	216	29.202	9.375	43.865	1.00	19.68	8
ATOM	1608	CB	ASN	A	216	31.049	8.938	41.893	1.00	15.86	6
ATOM	1609	CG	ASN	A	216	31.212	7.736	42.799	1.00	19.49	6
ATOM	1610	OD1	ASN	A	216	30.528	6.722	42.724	1.00	15.44	8
ATOM	1611	ND2	ASN	A	216	32.178	7.841	43.735	1.00	22.33	7
ATOM	1612	N	GLY	A	217	27.452	9.740	42.450	1.00	15.37	7
ATOM	1613	CA	GLY	A	217	26.528	10.146	43.484	1.00	15.63	6
ATOM	1614	C	GLY	A	217	25.397	9.108	43.658	1.00	12.67	6
ATOM	1615	O	GLY	A	217	25.274	8.223	42.830	1.00	13.61	8
ATOM	1616	N	TYR	A	218	24.763	9.167	44.820	1.00	14.53	7
ATOM	1617	CA	TYR	A	218	23.540	8.474	45.147	1.00	13.47	6
ATOM	1618	C	TYR	A	218	22.573	9.467	45.748	1.00	17.36	6
ATOM	1619	O	TYR	A	218	23.042	10.313	46.555	1.00	19.27	8
ATOM	1620	CB	TYR	A	218	23.781	7.308	46.161	1.00	11.47	6
ATOM	1621	CG	TYR	A	218	24.809	6.356	45.591	1.00	12.20	6

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ATOM   1622  CD1 TYR A 218      26.208   6.488  45.773  1.00 13.37   6
ATOM   1623  CD2 TYR A 218      24.426   5.277  44.820  1.00 12.84   6
ATOM   1624  CE1 TYR A 218      27.084   5.638  45.230  1.00 13.51   6
ATOM   1625  CE2 TYR A 218      25.300   4.451  44.233  1.00 11.27   6
ATOM   1626  CZ  TYR A 218      26.691   4.566  44.425  1.00 11.33   6
ATOM   1627  OH  TYR A 218      27.563   3.704  43.856  1.00 14.19   8
ATOM   1628  N   SER A 219      21.302   9.383  45.406  1.00 13.70   7
ATOM   1629  CA  SER A 219      20.345  10.292  45.991  1.00 12.43   6
ATOM   1630  C   SER A 219      18.946   9.690  45.979  1.00 12.57   6
ATOM   1631  O   SER A 219      18.687   8.690  45.259  1.00 11.67   8
ATOM   1632  CB  SER A 219      20.380  11.571  45.175  1.00 16.94   6
ATOM   1633  OG  SER A 219      19.543  11.401  44.030  1.00 27.04   8
ATOM   1634  N   TYR A 220      18.080  10.236  46.794  1.00 11.86   7
ATOM   1635  CA  TYR A 220      16.690   9.896  46.724  1.00 11.51   6
ATOM   1636  C   TYR A 220      16.047  10.722  45.635  1.00 12.74   6
ATOM   1637  O   TYR A 220      16.188  11.953  45.508  1.00 13.70   8
ATOM   1638  CB  TYR A 220      16.005  10.337  48.053  1.00 11.07   6
ATOM   1639  CG  TYR A 220      16.356   9.479  49.223  1.00 15.23   6
ATOM   1640  CD1 TYR A 220      16.096   8.130  49.290  1.00 12.19   6
ATOM   1641  CD2 TYR A 220      16.970  10.065  50.348  1.00 20.94   6
ATOM   1642  CE1 TYR A 220      16.418   7.319  50.363  1.00 17.15   6
ATOM   1643  CE2 TYR A 220      17.282   9.257  51.432  1.00 20.63   6
ATOM   1644  CZ  TYR A 220      17.013   7.927  51.455  1.00 20.24   6
ATOM   1645  OH  TYR A 220      17.330   7.134  52.548  1.00 22.60   8
ATOM   1646  N   MET A 221      15.085  10.098  44.923  1.00 12.98   7
ATOM   1647  CA  MET A 221      14.179  10.786  43.985  1.00 10.83   6
ATOM   1648  C   MET A 221      12.794  10.191  44.197  1.00 10.00   6
ATOM   1649  O   MET A 221      12.691   9.016  44.620  1.00 11.94   8
ATOM   1650  CB  MET A 221      14.581  10.675  42.492  1.00 12.31   6
ATOM   1651  CG  MET A 221      15.728  11.611  42.190  1.00 13.70   6
ATOM   1652  SD  MET A 221      15.997  11.530  40.390  1.00 15.78  16
ATOM   1653  CE  MET A 221      17.585  12.292  40.256  1.00 23.46   6
ATOM   1654  N   SER A 222      11.723  10.901  43.905  1.00 10.92   7
ATOM   1655  CA  SER A 222      10.357  10.422  44.042  1.00  9.76   6
ATOM   1656  C   SER A 222       9.586  10.751  42.758  1.00 12.04   6
ATOM   1657  O   SER A 222       9.755  11.827  42.185  1.00 15.35   8
ATOM   1658  CB  SER A 222       9.609  11.100  45.197  1.00 14.86   6
ATOM   1659  OG  SER A 222      10.216  10.861  46.463  1.00 13.78   8
ATOM   1660  N   GLY A 223       8.779   9.812  42.394  1.00 12.72   7
ATOM   1661  CA  GLY A 223       7.819  10.014  41.264  1.00 15.17   6
ATOM   1662  C   GLY A 223       7.505   8.657  40.630  1.00 10.31   6
ATOM   1663  O   GLY A 223       8.041   7.604  40.919  1.00 11.61   8
ATOM   1664  N   THR A 224       6.499   8.863  39.717  1.00 10.35   7
ATOM   1665  CA  THR A 224       6.175   7.685  38.909  1.00  8.89   6
ATOM   1666  C   THR A 224       7.383   7.335  38.027  1.00  9.98   6
ATOM   1667  O   THR A 224       7.487   6.168  37.607  1.00  9.81   8
ATOM   1668  CB  THR A 224       4.920   7.788  38.038  1.00  8.97   6
ATOM   1669  OG1 THR A 224       5.026   8.958  37.216  1.00 11.03   8
ATOM   1670  CG2 THR A 224       3.671   7.909  38.950  1.00  9.27   6
ATOM   1671  N   SER A 225       8.317   8.243  37.735  1.00 10.17   7
ATOM   1672  CA  SER A 225       9.552   7.955  37.067  1.00 11.35   6
ATOM   1673  C   SER A 225      10.427   6.946  37.830  1.00  8.09   6
ATOM   1674  O   SER A 225      11.258   6.285  37.163  1.00  8.80   8
ATOM   1675  CB  SER A 225      10.482   9.186  36.881  1.00 12.32   6
ATOM   1676  OG  SER A 225       9.832  10.043  35.881  1.00 13.46   8
ATOM   1677  N   MET A 226      10.191   6.844  39.146  1.00  8.91   7
ATOM   1678  CA  MET A 226      10.978   5.898  39.914  1.00  9.87   6
ATOM   1679  C   MET A 226      10.277   4.558  40.071  1.00  8.01   6
ATOM   1680  O   MET A 226      10.852   3.512  40.318  1.00 10.42   8
ATOM   1681  CB  MET A 226      11.246   6.476  41.336  1.00 10.18   6
ATOM   1682  CG  MET A 226      12.310   7.569  41.381  1.00  9.98   6
ATOM   1683  SD  MET A 226      11.911   9.112  40.574  1.00 11.41  16
ATOM   1684  CE  MET A 226      13.090   8.930  39.205  1.00 13.09   6
ATOM   1685  N   ALA A 227       8.939   4.581  39.923  1.00  9.49   7
ATOM   1686  CA  ALA A 227       8.136   3.349  40.019  1.00  9.59   6
ATOM   1687  C   ALA A 227       8.327   2.524  38.724  1.00  8.92   6
ATOM   1688  O   ALA A 227       8.449   1.279  38.759  1.00  9.60   8
ATOM   1689  CB  ALA A 227       6.684   3.754  40.239  1.00 12.00   6
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ATOM	1690	N	SER	A	228	8.258	3.251	37.598	1.00	8.46	7
ATOM	1691	CA	SER	A	228	8.366	2.564	36.293	1.00	9.33	6
ATOM	1692	C	SER	A	228	9.597	1.685	36.177	1.00	9.11	6
ATOM	1693	O	SER	A	228	9.393	0.525	35.768	1.00	8.88	8
ATOM	1694	CB	SER	A	228	8.311	3.644	35.222	1.00	8.72	6
ATOM	1695	OG	SER	A	228	8.326	3.035	33.893	1.00	8.59	8
ATOM	1696	N	PRO	A	229	10.790	2.071	36.569	1.00	9.43	7
ATOM	1697	CA	PRO	A	229	11.941	1.221	36.420	1.00	9.18	6
ATOM	1698	C	PRO	A	229	11.901	-0.018	37.312	1.00	9.20	6
ATOM	1699	O	PRO	A	229	12.519	-1.041	37.077	1.00	10.50	8
ATOM	1700	CB	PRO	A	229	13.198	2.065	36.744	1.00	10.68	6
ATOM	1701	CG	PRO	A	229	12.614	3.303	37.459	1.00	10.44	6
ATOM	1702	CD	PRO	A	229	11.196	3.448	36.832	1.00	10.93	6
ATOM	1703	N	HIS	A	230	11.144	0.079	38.459	1.00	8.14	7
ATOM	1704	CA	HIS	A	230	10.984	-1.193	39.194	1.00	8.04	6
ATOM	1705	C	HIS	A	230	10.199	-2.229	38.398	1.00	8.61	6
ATOM	1706	O	HIS	A	230	10.502	-3.422	38.383	1.00	11.42	8
ATOM	1707	CB	HIS	A	230	10.245	-0.952	40.567	1.00	8.82	6
ATOM	1708	CG	HIS	A	230	11.092	-0.269	41.632	1.00	7.05	6
ATOM	1709	ND1	HIS	A	230	11.161	1.109	41.777	1.00	7.95	7
ATOM	1710	CD2	HIS	A	230	11.925	-0.847	42.579	1.00	10.46	6
ATOM	1711	CE1	HIS	A	230	12.001	1.359	42.791	1.00	11.65	6
ATOM	1712	NE2	HIS	A	230	12.464	0.188	43.283	1.00	10.70	7
ATOM	1713	N	VAL	A	231	9.136	-1.757	37.702	1.00	9.27	7
ATOM	1714	CA	VAL	A	231	8.379	-2.623	36.808	1.00	9.26	6
ATOM	1715	C	VAL	A	231	9.199	-3.052	35.601	1.00	8.69	6
ATOM	1716	O	VAL	A	231	9.159	-4.237	35.255	1.00	9.29	8
ATOM	1717	CB	VAL	A	231	7.078	-1.927	36.389	1.00	8.06	6
ATOM	1718	CG1	VAL	A	231	6.310	-2.873	35.444	1.00	12.86	6
ATOM	1719	CG2	VAL	A	231	6.254	-1.603	37.646	1.00	9.44	6
ATOM	1720	N	ALA	A	232	9.967	-2.118	35.010	1.00	8.72	7
ATOM	1721	CA	ALA	A	232	10.810	-2.548	33.900	1.00	9.54	6
ATOM	1722	C	ALA	A	232	11.885	-3.530	34.291	1.00	9.30	6
ATOM	1723	O	ALA	A	232	12.173	-4.505	33.567	1.00	9.44	8
ATOM	1724	CB	ALA	A	232	11.466	-1.262	33.299	1.00	10.48	6
ATOM	1725	N	GLY	A	233	12.382	-3.408	35.553	1.00	9.18	7
ATOM	1726	CA	GLY	A	233	13.367	-4.396	36.019	1.00	9.95	6
ATOM	1727	C	GLY	A	233	12.770	-5.794	36.214	1.00	8.05	6
ATOM	1728	O	GLY	A	233	13.315	-6.802	35.870	1.00	9.80	8
ATOM	1729	N	LEU	A	234	11.543	-5.846	36.799	1.00	8.56	7
ATOM	1730	CA	LEU	A	234	10.797	-7.116	36.861	1.00	9.22	6
ATOM	1731	C	LEU	A	234	10.564	-7.685	35.452	1.00	8.93	6
ATOM	1732	O	LEU	A	234	10.703	-8.869	35.257	1.00	11.08	8
ATOM	1733	CB	LEU	A	234	9.502	-6.924	37.673	1.00	10.61	6
ATOM	1734	CG	LEU	A	234	8.527	-8.118	37.675	1.00	10.54	6
ATOM	1735	CD1	LEU	A	234	9.338	-9.334	38.172	1.00	10.76	6
ATOM	1736	CD2	LEU	A	234	7.332	-7.778	38.516	1.00	11.53	6
ATOM	1737	N	ALA	A	235	10.192	-6.794	34.514	1.00	8.31	7
ATOM	1738	CA	ALA	A	235	9.995	-7.321	33.159	1.00	9.02	6
ATOM	1739	C	ALA	A	235	11.282	-7.907	32.638	1.00	9.50	6
ATOM	1740	O	ALA	A	235	11.236	-8.925	31.905	1.00	9.26	8
ATOM	1741	CB	ALA	A	235	9.452	-6.193	32.283	1.00	8.43	6
ATOM	1742	N	ALA	A	236	12.423	-7.302	32.983	1.00	9.58	7
ATOM	1743	CA	ALA	A	236	13.686	-7.893	32.481	1.00	10.25	6
ATOM	1744	C	ALA	A	236	13.951	-9.229	33.200	1.00	9.83	6
ATOM	1745	O	ALA	A	236	14.536	-10.134	32.561	1.00	11.26	8
ATOM	1746	CB	ALA	A	236	14.866	-6.960	32.777	1.00	11.37	6
ATOM	1747	N	LEU	A	237	13.560	-9.388	34.455	1.00	10.12	7
ATOM	1748	CA	LEU	A	237	13.759	-10.691	35.102	1.00	11.28	6
ATOM	1749	C	LEU	A	237	12.950	-11.749	34.387	1.00	11.62	6
ATOM	1750	O	LEU	A	237	13.438	-12.838	34.062	1.00	11.77	8
ATOM	1751	CB	LEU	A	237	13.237	-10.615	36.577	1.00	9.89	6
ATOM	1752	CG	LEU	A	237	14.114	-9.812	37.528	1.00	10.68	6
ATOM	1753	CD1	LEU	A	237	13.489	-9.905	38.936	1.00	10.83	6
ATOM	1754	CD2	LEU	A	237	15.587	-10.206	37.543	1.00	12.79	6
ATOM	1755	N	LEU	A	238	11.724	-11.386	34.007	1.00	10.46	7
ATOM	1756	CA	LEU	A	238	10.866	-12.313	33.258	1.00	10.34	6
ATOM	1757	C	LEU	A	238	11.442	-12.561	31.856	1.00	11.39	6

ATOM	1758	O	LEU	A	238	11.368	-13.727	31.401	1.00	11.82	8
ATOM	1759	CB	LEU	A	238	9.446	-11.747	33.253	1.00	11.04	6
ATOM	1760	CG	LEU	A	238	8.748	-11.652	34.596	1.00	9.18	6
ATOM	1761	CD1	LEU	A	238	7.624	-10.610	34.653	1.00	13.12	6
ATOM	1762	CD2	LEU	A	238	8.198	-13.037	34.992	1.00	14.13	6
ATOM	1763	N	ALA	A	239	11.985	-11.570	31.187	1.00	11.41	7
ATOM	1764	CA	ALA	A	239	12.536	-11.834	29.836	1.00	11.12	6
ATOM	1765	C	ALA	A	239	13.707	-12.810	29.917	1.00	13.22	6
ATOM	1766	O	ALA	A	239	13.904	-13.584	28.964	1.00	14.69	8
ATOM	1767	CB	ALA	A	239	13.017	-10.507	29.271	1.00	11.43	6
ATOM	1768	N	SER	A	240	14.399	-12.833	31.034	1.00	10.04	7
ATOM	1769	CA	SER	A	240	15.560	-13.706	31.190	1.00	11.57	6
ATOM	1770	C	SER	A	240	15.069	-15.158	31.346	1.00	11.74	6
ATOM	1771	O	SER	A	240	15.978	-16.007	31.212	1.00	17.10	8
ATOM	1772	CB	SER	A	240	16.467	-13.253	32.339	1.00	15.20	6
ATOM	1773	OG	SER	A	240	15.907	-13.487	33.636	1.00	15.38	8
ATOM	1774	N	GLN	A	241	13.796	-15.390	31.539	1.00	12.24	7
ATOM	1775	CA	GLN	A	241	13.311	-16.765	31.686	1.00	13.26	6
ATOM	1776	C	GLN	A	241	12.864	-17.298	30.311	1.00	16.69	6
ATOM	1777	O	GLN	A	241	12.259	-18.381	30.257	1.00	17.39	8
ATOM	1778	CB	GLN	A	241	12.171	-16.794	32.671	1.00	12.49	6
ATOM	1779	CG	GLN	A	241	12.632	-16.408	34.116	1.00	14.22	6
ATOM	1780	CD	GLN	A	241	11.364	-16.351	34.927	1.00	14.64	6
ATOM	1781	OE1	GLN	A	241	10.413	-15.569	34.925	1.00	15.36	8
ATOM	1782	NE2	GLN	A	241	11.248	-17.409	35.756	1.00	14.32	7
ATOM	1783	N	GLY	A	242	13.086	-16.404	29.347	1.00	16.05	7
ATOM	1784	CA	GLY	A	242	12.689	-16.812	27.982	1.00	17.81	6
ATOM	1785	C	GLY	A	242	11.249	-16.549	27.658	1.00	18.23	6
ATOM	1786	O	GLY	A	242	10.619	-17.054	26.710	1.00	19.39	8
ATOM	1787	N	LYS	A	243	10.538	-15.778	28.476	1.00	15.28	7
ATOM	1788	CA	LYS	A	243	9.137	-15.458	28.344	1.00	12.91	6
ATOM	1789	C	LYS	A	243	9.010	-14.336	27.290	1.00	13.52	6
ATOM	1790	O	LYS	A	243	9.837	-13.408	27.296	1.00	16.08	8
ATOM	1791	CB	LYS	A	243	8.541	-14.995	29.664	1.00	15.99	6
ATOM	1792	CG	LYS	A	243	8.278	-16.185	30.633	1.00	16.79	6
ATOM	1793	CD	LYS	A	243	8.070	-15.687	32.070	1.00	21.08	6
ATOM	1794	CE	LYS	A	243	8.016	-17.016	32.871	1.00	25.90	6
ATOM	1795	NZ	LYS	A	243	8.276	-16.829	34.309	1.00	25.09	7
ATOM	1796	N	ASN	A	244	7.971	-14.396	26.458	1.00	12.59	7
ATOM	1797	CA	ASN	A	244	7.851	-13.360	25.428	1.00	12.14	6
ATOM	1798	C	ASN	A	244	7.060	-12.172	26.019	1.00	12.86	6
ATOM	1799	O	ASN	A	244	6.643	-12.195	27.204	1.00	12.30	8
ATOM	1800	CB	ASN	A	244	7.141	-13.969	24.225	1.00	11.92	6
ATOM	1801	CG	ASN	A	244	5.733	-14.363	24.487	1.00	14.11	6
ATOM	1802	OD1	ASN	A	244	4.907	-13.891	25.246	1.00	14.17	8
ATOM	1803	ND2	ASN	A	244	5.380	-15.450	23.740	1.00	25.93	7
ATOM	1804	N	ASN	A	245	6.779	-11.158	25.223	1.00	11.75	7
ATOM	1805	CA	ASN	A	245	6.231	-9.925	25.803	1.00	12.32	6
ATOM	1806	C	ASN	A	245	4.838	-10.185	26.373	1.00	11.73	6
ATOM	1807	O	ASN	A	245	4.488	-9.607	27.389	1.00	11.85	8
ATOM	1808	CB	ASN	A	245	6.266	-8.706	24.917	1.00	9.82	6
ATOM	1809	CG	ASN	A	245	5.639	-8.895	23.503	1.00	11.05	6
ATOM	1810	OD1	ASN	A	245	5.182	-9.975	23.141	1.00	12.49	8
ATOM	1811	ND2	ASN	A	245	5.668	-7.759	22.832	1.00	11.22	7
ATOM	1812	N	VAL	A	246	4.041	-10.938	25.608	1.00	12.28	7
ATOM	1813	CA	VAL	A	246	2.701	-11.231	26.102	1.00	11.50	6
ATOM	1814	C	VAL	A	246	2.798	-11.932	27.464	1.00	12.02	6
ATOM	1815	O	VAL	A	246	2.046	-11.541	28.399	1.00	13.42	8
ATOM	1816	CB	VAL	A	246	1.936	-12.088	25.084	1.00	13.60	6
ATOM	1817	CG1	VAL	A	246	0.562	-12.527	25.579	1.00	17.63	6
ATOM	1818	CG2	VAL	A	246	1.693	-11.266	23.802	1.00	15.00	6
ATOM	1819	N	GLN	A	247	3.644	-12.913	27.577	1.00	13.17	7
ATOM	1820	CA	GLN	A	247	3.880	-13.682	28.797	1.00	12.37	6
ATOM	1821	C	GLN	A	247	4.332	-12.767	29.958	1.00	13.38	6
ATOM	1822	O	GLN	A	247	3.853	-12.922	31.081	1.00	13.69	8
ATOM	1823	CB	GLN	A	247	4.936	-14.778	28.529	1.00	14.20	6
ATOM	1824	CG	GLN	A	247	4.208	-15.911	27.719	1.00	16.06	6
ATOM	1825	CD	GLN	A	247	5.269	-16.941	27.390	1.00	19.34	6

ATOM	1826	OE1	GLN	A	247	6.402	-16.706	27.042	1.00	16.30	8
ATOM	1827	NE2	GLN	A	247	4.878	-18.224	27.535	1.00	34.55	7
ATOM	1828	N	ILE	A	248	5.310	-11.937	29.616	1.00	11.49	7
ATOM	1829	CA	ILE	A	248	5.861	-10.997	30.646	1.00	9.94	6
ATOM	1830	C	ILE	A	248	4.771	-10.099	31.209	1.00	13.72	6
ATOM	1831	O	ILE	A	248	4.620	-9.931	32.436	1.00	10.62	8
ATOM	1832	CB	ILE	A	248	6.992	-10.169	30.002	1.00	9.93	6
ATOM	1833	CG1	ILE	A	248	8.162	-11.067	29.687	1.00	12.15	6
ATOM	1834	CG2	ILE	A	248	7.433	-9.060	30.990	1.00	12.79	6
ATOM	1835	CD1	ILE	A	248	9.257	-10.336	28.894	1.00	12.72	6
ATOM	1836	N	ARG	A	249	4.049	-9.408	30.310	1.00	11.43	7
ATOM	1837	CA	ARG	A	249	3.025	-8.484	30.767	1.00	10.98	6
ATOM	1838	C	ARG	A	249	1.907	-9.207	31.499	1.00	10.67	6
ATOM	1839	O	ARG	A	249	1.515	-8.692	32.585	1.00	12.16	8
ATOM	1840	CB	ARG	A	249	2.523	-7.745	29.486	1.00	12.64	6
ATOM	1841	CG	ARG	A	249	1.422	-6.790	30.009	1.00	14.83	6
ATOM	1842	CD	ARG	A	249	0.941	-5.857	28.893	1.00	11.70	6
ATOM	1843	NE	ARG	A	249	0.026	-4.852	29.485	1.00	12.16	7
ATOM	1844	CZ	ARG	A	249	-0.233	-3.681	28.909	1.00	17.32	6
ATOM	1845	NH1	ARG	A	249	0.242	-3.351	27.697	1.00	12.81	7
ATOM	1846	NH2	ARG	A	249	-1.008	-2.825	29.582	1.00	17.64	7
ATOM	1847	N	GLN	A	250	1.444	-10.388	31.087	1.00	12.08	7
ATOM	1848	CA	GLN	A	250	0.444	-11.146	31.801	1.00	12.15	6
ATOM	1849	C	GLN	A	250	0.953	-11.527	33.183	1.00	12.65	6
ATOM	1850	O	GLN	A	250	0.181	-11.410	34.154	1.00	13.71	8
ATOM	1851	CB	GLN	A	250	0.049	-12.401	30.982	1.00	13.50	6
ATOM	1852	CG	GLN	A	250	-1.139	-13.177	31.520	1.00	25.34	6
ATOM	1853	CD	GLN	A	250	-1.654	-14.042	30.351	1.00	34.38	6
ATOM	1854	OE1	GLN	A	250	-0.926	-14.231	29.379	1.00	40.16	8
ATOM	1855	NE2	GLN	A	250	-2.883	-14.525	30.453	1.00	47.06	7
ATOM	1856	N	ALA	A	251	2.236	-11.906	33.278	1.00	10.23	7
ATOM	1857	CA	ALA	A	251	2.706	-12.323	34.620	1.00	12.97	6
ATOM	1858	C	ALA	A	251	2.739	-11.135	35.535	1.00	12.84	6
ATOM	1859	O	ALA	A	251	2.312	-11.212	36.717	1.00	12.96	8
ATOM	1860	CB	ALA	A	251	4.077	-12.957	34.470	1.00	14.38	6
ATOM	1861	N	ILE	A	252	3.171	-9.986	35.045	1.00	11.02	7
ATOM	1862	CA	ILE	A	252	3.233	-8.795	35.947	1.00	10.23	6
ATOM	1863	C	ILE	A	252	1.845	-8.365	36.406	1.00	10.23	6
ATOM	1864	O	ILE	A	252	1.633	-8.028	37.616	1.00	13.67	8
ATOM	1865	CB	ILE	A	252	3.878	-7.669	35.112	1.00	12.15	6
ATOM	1866	CG1	ILE	A	252	5.396	-7.885	34.981	1.00	11.82	6
ATOM	1867	CG2	ILE	A	252	3.648	-6.337	35.843	1.00	13.44	6
ATOM	1868	CD1	ILE	A	252	6.044	-6.969	33.949	1.00	13.14	6
ATOM	1869	N	GLU	A	253	0.879	-8.376	35.492	1.00	12.32	7
ATOM	1870	CA	GLU	A	253	-0.446	-7.831	35.833	1.00	13.24	6
ATOM	1871	C	GLU	A	253	-1.237	-8.841	36.640	1.00	12.78	6
ATOM	1872	O	GLU	A	253	-1.895	-8.507	37.621	1.00	15.59	8
ATOM	1873	CB	GLU	A	253	-1.189	-7.514	34.507	1.00	11.47	6
ATOM	1874	CG	GLU	A	253	-0.638	-6.220	33.908	1.00	11.43	6
ATOM	1875	CD	GLU	A	253	-1.256	-5.936	32.527	1.00	15.21	6
ATOM	1876	OE1	GLU	A	253	-1.899	-6.803	31.926	1.00	18.21	8
ATOM	1877	OE2	GLU	A	253	-1.005	-4.753	32.206	1.00	17.23	8
ATOM	1878	N	GLN	A	254	-1.220	-10.134	36.212	1.00	12.34	7
ATOM	1879	CA	GLN	A	254	-2.095	-11.122	36.842	1.00	13.43	6
ATOM	1880	C	GLN	A	254	-1.626	-11.501	38.222	1.00	13.73	6
ATOM	1881	O	GLN	A	254	-2.499	-11.966	39.024	1.00	19.17	8
ATOM	1882	CB	GLN	A	254	-2.151	-12.364	35.966	1.00	14.03	6
ATOM	1883	CG	GLN	A	254	-2.890	-12.159	34.651	1.00	15.03	6
ATOM	1884	CD	GLN	A	254	-4.361	-11.906	34.885	1.00	16.67	6
ATOM	1885	OE1	GLN	A	254	-5.113	-12.665	35.520	1.00	18.71	8
ATOM	1886	NE2	GLN	A	254	-4.734	-10.738	34.346	1.00	19.67	7
ATOM	1887	N	THR	A	255	-0.340	-11.323	38.570	1.00	12.59	7
ATOM	1888	CA	THR	A	255	0.078	-11.666	39.938	1.00	12.50	6
ATOM	1889	C	THR	A	255	0.218	-10.480	40.876	1.00	11.92	6
ATOM	1890	O	THR	A	255	0.652	-10.698	41.999	1.00	13.55	8
ATOM	1891	CB	THR	A	255	1.449	-12.367	39.919	1.00	11.55	6
ATOM	1892	OG1	THR	A	255	2.490	-11.507	39.357	1.00	12.19	8
ATOM	1893	CG2	THR	A	255	1.423	-13.635	39.054	1.00	12.96	6

ATOM	1894	N	ALA	A	256	-0.211	-9.309	40.417	1.00	12.42	7
ATOM	1895	CA	ALA	A	256	0.004	-8.131	41.307	1.00	11.98	6
ATOM	1896	C	ALA	A	256	-0.832	-8.313	42.563	1.00	13.19	6
ATOM	1897	O	ALA	A	256	-1.957	-8.835	42.505	1.00	15.40	8
ATOM	1898	CB	ALA	A	256	-0.438	-6.931	40.502	1.00	13.07	6
ATOM	1899	N	ASP	A	257	-0.266	-7.824	43.683	1.00	10.82	7
ATOM	1900	CA	ASP	A	257	-1.023	-7.893	44.954	1.00	11.39	6
ATOM	1901	C	ASP	A	257	-2.151	-6.879	44.921	1.00	12.69	6
ATOM	1902	O	ASP	A	257	-1.949	-5.658	44.672	1.00	12.22	8
ATOM	1903	CB	ASP	A	257	-0.048	-7.519	46.064	1.00	12.06	6
ATOM	1904	CG	ASP	A	257	0.966	-8.615	46.339	1.00	14.17	6
ATOM	1905	OD1	ASP	A	257	0.623	-9.774	46.083	1.00	17.70	8
ATOM	1906	OD2	ASP	A	257	2.038	-8.290	46.893	1.00	18.13	8
ATOM	1907	N	LYS	A	258	-3.323	-7.323	45.341	1.00	12.79	7
ATOM	1908	CA	LYS	A	258	-4.489	-6.445	45.358	1.00	13.57	6
ATOM	1909	C	LYS	A	258	-4.583	-5.594	46.592	1.00	14.49	6
ATOM	1910	O	LYS	A	258	-5.543	-5.711	47.389	1.00	16.26	8
ATOM	1911	CB	LYS	A	258	-5.790	-7.213	45.052	1.00	17.86	6
ATOM	1912	CG	LYS	A	258	-5.563	-7.937	43.706	1.00	22.99	6
ATOM	1913	CD	LYS	A	258	-6.836	-8.271	42.954	1.00	27.90	6
ATOM	1914	CE	LYS	A	258	-6.527	-9.082	41.707	1.00	24.57	6
ATOM	1915	NZ	LYS	A	258	-5.879	-8.283	40.605	1.00	25.24	7
ATOM	1916	N	ILE	A	259	-3.678	-4.648	46.756	1.00	15.10	7
ATOM	1917	CA	ILE	A	259	-3.576	-3.775	47.898	1.00	13.74	6
ATOM	1918	C	ILE	A	259	-4.677	-2.717	47.867	1.00	13.04	6
ATOM	1919	O	ILE	A	259	-5.360	-2.579	46.845	1.00	12.63	8
ATOM	1920	CB	ILE	A	259	-2.175	-3.096	47.981	1.00	14.87	6
ATOM	1921	CG1	ILE	A	259	-1.974	-2.187	46.764	1.00	14.73	6
ATOM	1922	CG2	ILE	A	259	-1.086	-4.132	48.153	1.00	13.52	6
ATOM	1923	CD1	ILE	A	259	-0.796	-1.246	46.901	1.00	14.29	6
ATOM	1924	N	SER	A	260	-4.840	-1.987	48.985	1.00	13.66	7
ATOM	1925	CA	SER	A	260	-5.820	-0.905	48.928	1.00	13.91	6
ATOM	1926	C	SER	A	260	-5.545	0.022	47.760	1.00	14.86	6
ATOM	1927	O	SER	A	260	-4.392	0.338	47.415	1.00	15.35	8
ATOM	1928	CB	SER	A	260	-5.652	-0.158	50.271	1.00	23.45	6
ATOM	1929	OG	SER	A	260	-6.523	0.961	50.264	1.00	32.81	8
ATOM	1930	N	GLY	A	261	-6.615	0.415	47.065	1.00	14.79	7
ATOM	1931	CA	GLY	A	261	-6.451	1.204	45.853	1.00	15.91	6
ATOM	1932	C	GLY	A	261	-6.756	0.360	44.617	1.00	12.68	6
ATOM	1933	O	GLY	A	261	-6.863	0.965	43.534	1.00	12.20	8
ATOM	1934	N	THR	A	262	-6.655	-0.924	44.705	1.00	12.44	7
ATOM	1935	CA	THR	A	262	-6.915	-1.796	43.537	1.00	10.57	6
ATOM	1936	C	THR	A	262	-8.331	-1.542	43.030	1.00	13.90	6
ATOM	1937	O	THR	A	262	-9.301	-1.632	43.819	1.00	15.95	8
ATOM	1938	CB	THR	A	262	-6.699	-3.286	43.840	1.00	13.48	6
ATOM	1939	OG1	THR	A	262	-5.331	-3.420	44.229	1.00	14.15	8
ATOM	1940	CG2	THR	A	262	-6.959	-4.137	42.617	1.00	16.51	6
ATOM	1941	N	GLY	A	263	-8.396	-1.179	41.747	1.00	11.09	7
ATOM	1942	CA	GLY	A	263	-9.735	-0.902	41.152	1.00	12.45	6
ATOM	1943	C	GLY	A	263	-10.071	0.568	41.158	1.00	11.46	6
ATOM	1944	O	GLY	A	263	-10.990	1.093	40.464	1.00	14.08	8
ATOM	1945	N	THR	A	264	-9.309	1.422	41.872	1.00	10.76	7
ATOM	1946	CA	THR	A	264	-9.488	2.859	41.933	1.00	10.53	6
ATOM	1947	C	THR	A	264	-8.266	3.602	41.401	1.00	11.33	6
ATOM	1948	O	THR	A	264	-8.356	4.471	40.518	1.00	13.25	8
ATOM	1949	CB	ATHR	A	264	-9.810	3.214	43.400	0.50	13.28	6
ATOM	1950	OG1	ATHR	A	264	-10.941	2.511	43.897	0.50	13.13	8
ATOM	1951	CG2	ATHR	A	264	-9.919	4.711	43.436	0.50	8.33	6
ATOM	1952	CB	BTHR	A	264	-9.844	3.467	43.308	0.50	11.69	6
ATOM	1953	OG1	BTHR	A	264	-8.956	2.998	44.344	0.50	11.80	8
ATOM	1954	CG2	BTHR	A	264	-11.253	3.162	43.724	0.50	10.13	6
ATOM	1955	N	ASN	A	265	-7.080	3.363	42.000	1.00	10.66	7
ATOM	1956	CA	ASN	A	265	-5.841	4.057	41.612	1.00	10.59	6
ATOM	1957	C	ASN	A	265	-5.059	3.298	40.573	1.00	11.52	6
ATOM	1958	O	ASN	A	265	-4.186	3.892	39.906	1.00	11.50	8
ATOM	1959	CB	ASN	A	265	-4.983	4.241	42.859	1.00	11.37	6
ATOM	1960	CG	ASN	A	265	-5.590	5.258	43.826	1.00	12.28	6
ATOM	1961	OD1	ASN	A	265	-6.418	6.059	43.416	1.00	15.68	8

ATOM	1962	ND2	ASN	A	265	-5.153	5.175	45.083	1.00	16.82	7
ATOM	1963	N	PHE	A	266	-5.368	2.029	40.370	1.00	12.07	7
ATOM	1964	CA	PHE	A	266	-4.728	1.230	39.337	1.00	13.47	6
ATOM	1965	C	PHE	A	266	-5.576	-0.003	39.144	1.00	11.98	6
ATOM	1966	O	PHE	A	266	-6.414	-0.342	40.025	1.00	13.68	8
ATOM	1967	CB	PHE	A	266	-3.273	0.833	39.743	1.00	11.51	6
ATOM	1968	CG	PHE	A	266	-3.191	0.624	41.228	1.00	10.99	6
ATOM	1969	CD1	PHE	A	266	-2.709	1.603	42.034	1.00	12.36	6
ATOM	1970	CD2	PHE	A	266	-3.617	-0.589	41.768	1.00	12.87	6
ATOM	1971	CE1	PHE	A	266	-2.646	1.489	43.437	1.00	15.18	6
ATOM	1972	CE2	PHE	A	266	-3.548	-0.720	43.157	1.00	13.50	6
ATOM	1973	CZ	PHE	A	266	-3.086	0.299	43.954	1.00	13.91	6
ATOM	1974	N	LYS	A	267	-5.481	-0.713	38.018	1.00	10.86	7
ATOM	1975	CA	LYS	A	267	-6.372	-1.827	37.757	1.00	12.35	6
ATOM	1976	C	LYS	A	267	-5.996	-3.143	38.415	1.00	11.29	6
ATOM	1977	O	LYS	A	267	-6.827	-3.835	39.018	1.00	14.13	8
ATOM	1978	CB	LYS	A	267	-6.427	-2.056	36.234	1.00	10.21	6
ATOM	1979	CG	LYS	A	267	-7.269	-3.230	35.800	1.00	10.69	6
ATOM	1980	CD	LYS	A	267	-7.434	-3.314	34.277	1.00	17.41	6
ATOM	1981	CE	LYS	A	267	-8.125	-4.645	33.961	1.00	20.47	6
ATOM	1982	NZ	LYS	A	267	-9.590	-4.515	34.312	1.00	28.85	7
ATOM	1983	N	TYR	A	268	-4.703	-3.507	38.377	1.00	10.94	7
ATOM	1984	CA	TYR	A	268	-4.306	-4.845	38.774	1.00	10.54	6
ATOM	1985	C	TYR	A	268	-3.780	-4.934	40.185	1.00	12.48	6
ATOM	1986	O	TYR	A	268	-4.004	-5.966	40.828	1.00	14.47	8
ATOM	1987	CB	TYR	A	268	-3.247	-5.379	37.737	1.00	11.99	6
ATOM	1988	CG	TYR	A	268	-3.869	-5.582	36.354	1.00	12.59	6
ATOM	1989	CD1	TYR	A	268	-4.729	-6.636	36.098	1.00	17.30	6
ATOM	1990	CD2	TYR	A	268	-3.567	-4.713	35.315	1.00	11.77	6
ATOM	1991	CE1	TYR	A	268	-5.286	-6.819	34.836	1.00	16.83	6
ATOM	1992	CE2	TYR	A	268	-4.127	-4.878	34.044	1.00	14.50	6
ATOM	1993	CZ	TYR	A	268	-4.975	-5.940	33.842	1.00	16.27	6
ATOM	1994	OH	TYR	A	268	-5.578	-6.179	32.594	1.00	16.50	8
ATOM	1995	N	GLY	A	269	-2.951	-3.959	40.589	1.00	11.21	7
ATOM	1996	CA	GLY	A	269	-2.363	-4.068	41.950	1.00	11.42	6
ATOM	1997	C	GLY	A	269	-0.884	-3.640	41.935	1.00	12.63	6
ATOM	1998	O	GLY	A	269	-0.410	-2.979	40.981	1.00	12.33	8
ATOM	1999	N	LYS	A	270	-0.250	-3.975	43.039	1.00	10.84	7
ATOM	2000	CA	LYS	A	270	1.158	-3.689	43.298	1.00	10.02	6
ATOM	2001	C	LYS	A	270	1.989	-4.849	42.786	1.00	10.57	6
ATOM	2002	O	LYS	A	270	1.759	-6.030	43.116	1.00	10.24	8
ATOM	2003	CB	LYS	A	270	1.355	-3.550	44.835	1.00	9.80	6
ATOM	2004	CG	LYS	A	270	2.838	-3.440	45.234	1.00	10.47	6
ATOM	2005	CD	LYS	A	270	2.766	-3.574	46.792	1.00	13.93	6
ATOM	2006	CE	LYS	A	270	4.141	-3.882	47.323	1.00	13.15	6
ATOM	2007	NZ	LYS	A	270	4.141	-4.146	48.814	1.00	12.38	7
ATOM	2008	N	ILE	A	271	3.068	-4.553	41.981	1.00	9.21	7
ATOM	2009	CA	ILE	A	271	3.827	-5.684	41.486	1.00	10.54	6
ATOM	2010	C	ILE	A	271	4.345	-6.567	42.615	1.00	10.27	6
ATOM	2011	O	ILE	A	271	4.722	-6.097	43.676	1.00	10.76	8
ATOM	2012	CB	ILE	A	271	5.015	-5.309	40.579	1.00	9.40	6
ATOM	2013	CG1	ILE	A	271	5.942	-4.342	41.302	1.00	10.70	6
ATOM	2014	CG2	ILE	A	271	4.462	-4.651	39.299	1.00	12.37	6
ATOM	2015	CD1	ILE	A	271	7.353	-4.230	40.661	1.00	11.12	6
ATOM	2016	N	ASN	A	272	4.358	-7.864	42.304	1.00	11.32	7
ATOM	2017	CA	ASN	A	272	4.927	-8.895	43.187	1.00	11.90	6
ATOM	2018	C	ASN	A	272	5.887	-9.781	42.379	1.00	10.24	6
ATOM	2019	O	ASN	A	272	5.512	-10.582	41.534	1.00	11.33	8
ATOM	2020	CB	ASN	A	272	3.791	-9.719	43.774	1.00	10.81	6
ATOM	2021	CG	ASN	A	272	4.423	-10.703	44.785	1.00	13.73	6
ATOM	2022	OD1	ASN	A	272	5.449	-11.324	44.563	1.00	11.13	8
ATOM	2023	ND2	ASN	A	272	3.754	-10.772	45.915	1.00	15.82	7
ATOM	2024	N	SER	A	273	7.192	-9.406	42.462	1.00	11.18	7
ATOM	2025	CA	SER	A	273	8.176	-10.054	41.573	1.00	9.11	6
ATOM	2026	C	SER	A	273	8.243	-11.575	41.796	1.00	10.89	6
ATOM	2027	O	SER	A	273	8.463	-12.256	40.830	1.00	11.77	8
ATOM	2028	CB	SER	A	273	9.575	-9.501	41.899	1.00	12.03	6
ATOM	2029	OG	SER	A	273	9.574	-8.068	41.685	1.00	11.29	8

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ATOM   2030  N   ASN A 274       8.098 -11.968  43.092  1.00 11.68    7
ATOM   2031  CA  ASN A 274       8.221 -13.417  43.328  1.00 13.05    6
ATOM   2032  C   ASN A 274       7.075 -14.195  42.716  1.00 11.54    6
ATOM   2033  O   ASN A 274       7.388 -15.228  42.085  1.00 14.09    8
ATOM   2034  CB  ASN A 274       8.376 -13.678  44.846  1.00 13.98    6
ATOM   2035  CG  ASN A 274       8.826 -15.149  45.061  1.00 13.57    6
ATOM   2036  OD1 ASN A 274       9.757 -15.640  44.474  1.00 16.37    8
ATOM   2037  ND2 ASN A 274       8.018 -15.690  45.988  1.00 19.49    7
ATOM   2038  N   LYS A 275       5.882 -13.699  42.841  1.00 12.00    7
ATOM   2039  CA  LYS A 275       4.726 -14.366  42.195  1.00 11.46    6
ATOM   2040  C   LYS A 275       4.874 -14.299  40.667  1.00 12.56    6
ATOM   2041  O   LYS A 275       4.574 -15.288  40.002  1.00 12.54    8
ATOM   2042  CB  LYS A 275       3.383 -13.896  42.682  1.00 14.49    6
ATOM   2043  CG  LYS A 275       3.025 -13.902  44.182  1.00 17.77    6
ATOM   2044  CD  LYS A 275       1.573 -13.451  44.400  1.00 21.72    6
ATOM   2045  CE  LYS A 275       1.152 -12.015  44.481  1.00 28.84    6
ATOM   2046  NZ  LYS A 275      -0.267 -11.496  44.363  1.00 26.58    7
ATOM   2047  N   ALA A 276       5.310 -13.118  40.185  1.00 12.51    7
ATOM   2048  CA  ALA A 276       5.385 -13.059  38.706  1.00 10.12    6
ATOM   2049  C   ALA A 276       6.375 -14.014  38.107  1.00 10.25    6
ATOM   2050  O   ALA A 276       6.048 -14.635  37.070  1.00 10.48    8
ATOM   2051  CB  ALA A 276       5.743 -11.617  38.304  1.00 11.31    6
ATOM   2052  N   VAL A 277       7.553 -14.226  38.736  1.00 11.74    7
ATOM   2053  CA  VAL A 277       8.541 -15.041  38.026  1.00 10.78    6
ATOM   2054  C   VAL A 277       8.167 -16.518  38.194  1.00 14.27    6
ATOM   2055  O   VAL A 277       8.780 -17.298  37.504  1.00 13.97    8
ATOM   2056  CB  VAL A 277       9.970 -14.842  38.526  1.00 12.43    6
ATOM   2057  CG1 VAL A 277      10.448 -13.425  38.246  1.00 12.15    6
ATOM   2058  CG2 VAL A 277      10.184 -15.151  40.012  1.00 16.20    6
ATOM   2059  N   ARG A 278       7.190 -16.809  39.071  1.00 12.39    7
ATOM   2060  CA  ARG A 278       6.784 -18.223  39.175  1.00 15.11    6
ATOM   2061  C   ARG A 278       5.497 -18.504  38.446  1.00 16.59    6
ATOM   2062  O   ARG A 278       5.089 -19.689  38.350  1.00 20.78    8
ATOM   2063  CB  ARG A 278       6.542 -18.587  40.655  1.00 15.94    6
ATOM   2064  CG  ARG A 278       7.824 -18.422  41.383  1.00 17.42    6
ATOM   2065  CD  ARG A 278       7.595 -18.572  42.905  1.00 15.96    6
ATOM   2066  NE  ARG A 278       8.833 -18.230  43.559  1.00 19.66    7
ATOM   2067  CZ  ARG A 278       9.900 -18.901  43.897  1.00 24.54    6
ATOM   2068  NH1 ARG A 278       9.966 -20.223  43.611  1.00 23.93    7
ATOM   2069  NH2 ARG A 278      10.918 -18.305  44.529  1.00 26.20    7
ATOM   2070  N   TYR A 279       4.913 -17.490  37.831  1.00 12.78    7
ATOM   2071  CA  TYR A 279       3.644 -17.626  37.129  1.00 14.37    6
ATOM   2072  C   TYR A 279       3.850 -18.378  35.829  1.00 24.50    6
ATOM   2073  O   TYR A 279       4.901 -18.165  35.189  1.00 24.68    8
ATOM   2074  CB  TYR A 279       3.005 -16.277  36.932  1.00 13.65    6
ATOM   2075  CG  TYR A 279       1.693 -16.105  36.231  1.00 13.86    6
ATOM   2076  CD1 TYR A 279       0.452 -16.189  36.858  1.00 14.68    6
ATOM   2077  CD2 TYR A 279       1.736 -15.872  34.847  1.00 15.48    6
ATOM   2078  CE1 TYR A 279      -0.683 -16.037  36.103  1.00 15.73    6
ATOM   2079  CE2 TYR A 279       0.575 -15.702  34.121  1.00 14.88    6
ATOM   2080  CZ  TYR A 279      -0.652 -15.770  34.740  1.00 15.75    6
ATOM   2081  OH  TYR A 279      -1.834 -15.612  34.089  1.00 17.03    8
ATOM   2082  OT  TYR A 279       3.000 -19.258  35.525  1.00 24.50    8
ATOM   2083  C1  GLL A 296      -3.949   0.135  29.717  1.00 17.61    6
ATOM   2084  C2  GLL A 296      -4.024   1.580  29.221  1.00 16.18    6
ATOM   2085  C3  GLL A 296      -5.461   2.100  29.213  1.00 18.89    6
ATOM   2086  O1  GLL A 296      -2.578  -0.308  29.529  1.00 15.42    8
ATOM   2087  O2  GLL A 296      -3.163   2.400  30.001  1.00 15.61    8
ATOM   2088  O3  GLL A 296      -5.525   3.473  28.806  1.00 23.45    8
ATOM   2089 CA   WAT A   1      25.973  -1.842  43.443  1.00 11.05   20
ATOM   2090 CA   WAT A   2      25.647  13.399  23.751  1.00 17.24   20
ATOM   2091 NA   WAT A   3      -1.258   1.535  28.929  1.00 12.14   11
ATOM   2092  OW0 WAT W   4      16.838   2.112  43.195  1.00  9.07    8
ATOM   2093  OW0 WAT W   5      13.085   6.361  31.187  1.00 10.24    8
ATOM   2094  OW0 WAT W   6      18.887   0.537  42.447  1.00 10.28    8
ATOM   2095  OW0 WAT W   7      14.445   5.591  39.775  1.00 10.40    8
ATOM   2096  OW0 WAT W   8      14.210   1.611  47.107  1.00 10.59    8
ATOM   2097  OW0 WAT W   9      14.918   3.839  48.721  1.00 10.61    8
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ATOM	2098	OW0	WAT	W	10	10.698	-1.779	53.649	1.00	10.77	8	
ATOM	2099	OW0	WAT	W	11	-1.751	5.117	40.655	1.00	10.86	8	
ATOM	2100	OW0	WAT	W	12	14.945	0.687	44.697	1.00	10.99	8	
ATOM	2101	OW0	WAT	W	13	-0.327	4.307	42.978	1.00	11.25	8	
ATOM	2102	OW0	WAT	W	14	4.023	-3.345	27.168	1.00	11.76	8	
ATOM	2103	OW0	WAT	W	15	3.256	-8.810	39.822	1.00	11.88	8	
ATOM	2104	OW0	WAT	W	16	18.664	7.646	28.905	1.00	12.48	8	
ATOM	2105	OW0	WAT	W	17	29.275	-1.039	37.125	1.00	12.57	8	
ATOM	2106	OW0	WAT	W	18	20.255	15.290	29.790	1.00	12.74	8	
ATOM	2107	OW0	WAT	W	19	10.140	-8.862	25.520	1.00	12.92	8	
ATOM	2108	OW0	WAT	W	20	-1.402	0.794	22.084	1.00	13.07	8	
ATOM	2109	OW0	WAT	W	21	5.723	-0.410	49.244	1.00	13.11	8	
ATOM	2110	OW0	WAT	W	22	11.383	-11.545	49.015	1.00	13.37	8	
ATOM	2111	OW0	WAT	W	23	32.574	-0.530	38.835	1.00	13.78	8	
ATOM	2112	OW0	WAT	W	24	6.840	6.391	14.824	1.00	13.94	8	
ATOM	2113	OW0	WAT	W	25	4.270	-7.073	46.186	1.00	14.15	8	
ATOM	2114	OW0	WAT	W	26	16.914	-1.439	53.452	1.00	14.17	8	
ATOM	2115	OW0	WAT	W	27	25.377	-6.748	38.454	1.00	14.66	8	
ATOM	2116	OW0	WAT	W	28	16.613	-9.407	30.953	1.00	14.93	8	
ATOM	2117	OW0	WAT	W	29	3.879	7.957	30.204	1.00	14.99	8	
ATOM	2118	OW0	WAT	W	30	11.580	-4.612	12.085	1.00	15.06	8	
ATOM	2119	OW0	WAT	W	31	8.559	-11.110	22.717	1.00	15.31	8	
ATOM	2120	OW0	WAT	W	32	31.655	-2.825	39.954	1.00	15.39	8	
ATOM	2121	OW0	WAT	W	33	5.355	5.671	12.382	1.00	15.85	8	
ATOM	2122	OW0	WAT	W	34	14.542	5.167	15.017	1.00	15.88	8	
ATOM	2123	OW0	WAT	W	35	15.681	2.641	14.612	1.00	16.11	8	
ATOM	2124	OW0	WAT	W	36	22.959	-5.924	55.817	1.00	16.14	8	
ATOM	2125	OW0	WAT	W	37	17.792	-7.760	24.674	1.00	16.20	8	
ATOM	2126	OW0	WAT	W	38	-5.745	-0.511	32.819	1.00	16.38	8	
ATOM	2127	OW0	WAT	W	39	8.911	8.038	13.921	1.00	16.56	8	
ATOM	2128	OW0	WAT	W	40	0.345	-4.964	25.288	1.00	16.65	8	
ATOM	2129	OW0	WAT	W	41	11.031	-11.431	25.798	1.00	16.84	8	
ATOM	2130	OW0	WAT	W	42	13.079	5.575	51.582	1.00	17.00	8	
ATOM	2131	OW0	WAT	W	43	9.891	-5.124	53.560	1.00	17.04	8	
ATOM	2132	OW0	WAT	W	44	5.686	-8.148	48.229	1.00	17.09	8	
ATOM	2133	OW0	WAT	W	45	25.251	13.768	26.180	1.00	17.19	8	
ATOM	2134	OW0	WAT	W	46	-0.436	1.365	15.687	1.00	17.45	8	
ATOM	2135	OW0	WAT	W	47	-9.577	-3.555	38.689	1.00	17.51	8	
ATOM	2136	OW0	WAT	W	48	30.018	9.014	37.735	1.00	18.20	8	
ATOM	2137	OW0	WAT	W	49	15.370	-7.155	29.434	1.00	18.50	8	
ATOM	2138	OW0	WAT	W	50	20.118	20.536	34.111	1.00	18.97	8	
ATOM	2139	OW0	WAT	W	51	23.269	-5.467	51.272	1.00	19.01	8	
ATOM	2140	OW0	WAT	W	52	18.707	-18.348	45.501	1.00	19.39	8	
ATOM	2141	OW0	WAT	W	53	29.237	2.519	48.044	1.00	19.62	8	
ATOM	2142	OW0	WAT	W	54	-2.442	2.172	47.419	1.00	19.63	8	
ATOM	2143	OW0	WAT	W	55	19.933	-4.327	22.737	1.00	19.76	8	
ATOM	2144	OW0	WAT	W	56	34.473	-1.581	37.164	1.00	19.96	8	
ATOM	2145	OW0	WAT	W	57	12.821	11.824	47.078	1.00	20.13	8	
ATOM	2146	OW0	WAT	W	58	11.503	7.499	13.241	1.00	20.21	8	
ATOM	2147	OW0	WAT	W	59	23.684	-1.037	20.633	1.00	20.22	8	
ATOM	2148	OW0	WAT	W	60	-0.612	-3.323	51.692	1.00	20.28	8	
ATOM	2149	OW0	WAT	W	61	17.007	14.116	44.269	1.00	20.65	8	
ATOM	2150	OW0	WAT	W	62	-0.273	-9.571	27.817	1.00	20.67	8	
ATOM	2151	OW0	WAT	W	63	-11.316	-4.375	40.684	1.00	20.73	8	
ATOM	2152	OW0	WAT	W	64	25.755	-8.111	33.313	1.00	20.89	8	
ATOM	2153	OW0	WAT	W	65	-3.039	-2.283	51.281	1.00	20.99	8	
ATOM	2154	OW0	WAT	W	66	14.409	-8.631	51.937	1.00	20.99	8	
ATOM	2155	OW0	WAT	W	67	-3.784	-5.571	30.454	1.00	20.99	8	
ATOM	2156	OW0	WAT	W	68	28.701	0.916	24.873	1.00	21.03	8	
ATOM	2157	OW0	WAT	W	69	-2.298	4.090	45.230	1.00	21.11	8	
ATOM	2158	OW0	WAT	W	70	30.077	4.491	44.090	1.00	21.11	8	
ATOM	2159	OW0	WAT	W	71	-4.539	6.907	25.235	1.00	21.20	8	
ATOM	2160	OW0	WAT	W	72	7.930	16.602	17.863	1.00	21.38	8	
ATOM	2161	OW0	WAT	W	73	25.030	5.431	18.766	1.00	21.46	8	
ATOM	2162	OW0	WAT	W	74	21.967	-14.316	49.321	1.00	21.78	8	
ATOM	2163	OW0	WAT	W	75	2.376	-6.419	49.074	1.00	21.92	8	
ATOM	2164	OW0	WAT	W	76	4.085	10.456	48.716	1.00	22.11	8	
ATOM	2165	OW0	WAT	W	77	5.239	-12.232	48.334	1.00	22.25	8	

ATOM	2166	OW0	WAT	W	78	-4.190	-2.933	30.508	1.00	22.26	8
ATOM	2167	OW0	WAT	W	79	8.378	5.587	51.200	1.00	22.44	8
ATOM	2168	OW0	WAT	W	80	12.983	-5.518	20.760	1.00	22.55	8
ATOM	2169	OW0	WAT	W	81	9.499	10.528	14.890	1.00	22.84	8
ATOM	2170	OW0	WAT	W	82	2.960	-17.253	40.993	1.00	23.00	8
ATOM	2171	OW0	WAT	W	83	6.098	-15.849	34.785	1.00	23.11	8
ATOM	2172	OW0	WAT	W	84	-9.765	-5.816	36.844	1.00	23.23	8
ATOM	2173	OW0	WAT	W	85	17.165	-8.431	51.079	1.00	23.38	8
ATOM	2174	OW0	WAT	W	86	26.762	4.780	20.872	1.00	23.45	8
ATOM	2175	OW0	WAT	W	87	-3.582	-0.255	20.689	1.00	23.52	8
ATOM	2176	OW0	WAT	W	88	24.998	-0.493	54.746	1.00	23.60	8
ATOM	2177	OW0	WAT	W	89	15.378	4.977	52.842	1.00	23.62	8
ATOM	2178	OW0	WAT	W	90	-3.290	-9.213	32.314	1.00	23.62	8
ATOM	2179	OW0	WAT	W	91	-1.217	9.980	21.173	1.00	23.69	8
ATOM	2180	OW0	WAT	W	92	-4.575	5.139	23.029	1.00	23.74	8
ATOM	2181	OW0	WAT	W	93	5.660	-20.272	33.874	1.00	23.86	8
ATOM	2182	OW0	WAT	W	94	2.570	-19.717	32.700	1.00	23.93	8
ATOM	2183	OW0	WAT	W	95	-2.768	8.489	18.967	1.00	24.13	8
ATOM	2184	OW0	WAT	W	96	-9.884	0.662	45.427	1.00	24.32	8
ATOM	2185	OW0	WAT	W	97	5.619	-4.476	51.362	1.00	24.37	8
ATOM	2186	OW0	WAT	W	98	8.421	11.297	38.167	1.00	24.65	8
ATOM	2187	OW0	WAT	W	99	25.813	-8.535	52.635	1.00	24.70	8
ATOM	2188	OW0	WAT	W	100	20.832	19.605	26.661	1.00	24.82	8
ATOM	2189	OW0	WAT	W	101	16.258	-9.256	21.262	1.00	24.86	8
ATOM	2190	OW0	WAT	W	102	12.349	13.826	43.372	1.00	24.89	8
ATOM	2191	OW0	WAT	W	103	13.170	-19.745	35.451	1.00	24.90	8
ATOM	2192	OW0	WAT	W	104	7.075	17.770	20.578	1.00	24.93	8
ATOM	2193	OW0	WAT	W	105	22.242	-3.099	22.446	1.00	24.94	8
ATOM	2194	OW0	WAT	W	106	2.596	-15.349	31.525	1.00	25.01	8
ATOM	2195	OW0	WAT	W	107	13.138	-13.432	26.305	1.00	25.13	8
ATOM	2196	OW0	WAT	W	108	27.906	13.991	24.255	1.00	25.14	8
ATOM	2197	OW0	WAT	W	109	6.218	-4.057	14.703	1.00	25.22	8
ATOM	2198	OW0	WAT	W	110	10.505	12.665	32.677	1.00	25.29	8
ATOM	2199	OW0	WAT	W	111	-3.781	-2.725	27.641	1.00	25.30	8
ATOM	2200	OW0	WAT	W	112	30.677	10.964	34.167	1.00	25.31	8
ATOM	2201	OW0	WAT	W	113	17.661	-13.781	50.306	1.00	25.32	8
ATOM	2202	OW0	WAT	W	114	34.541	6.057	36.868	1.00	25.36	8
ATOM	2203	OW0	WAT	W	115	23.605	3.174	17.711	1.00	25.38	8
ATOM	2204	OW0	WAT	W	116	17.497	-13.278	24.578	1.00	25.43	8
ATOM	2205	OW0	WAT	W	117	26.337	-11.225	48.970	1.00	25.54	8
ATOM	2206	OW0	WAT	W	118	-5.239	13.734	29.361	1.00	25.59	8
ATOM	2207	OW0	WAT	W	119	-2.765	6.609	16.532	1.00	25.61	8
ATOM	2208	OW0	WAT	W	120	-0.782	-2.817	17.108	1.00	25.71	8
ATOM	2209	OW0	WAT	W	121	16.158	7.089	14.095	1.00	25.77	8
ATOM	2210	OW0	WAT	W	122	18.930	12.534	48.368	1.00	26.12	8
ATOM	2211	OW0	WAT	W	123	24.403	-6.067	53.444	1.00	26.65	8
ATOM	2212	OW0	WAT	W	124	-3.404	4.730	49.022	1.00	26.81	8
ATOM	2213	OW0	WAT	W	125	32.619	10.296	29.183	1.00	26.88	8
ATOM	2214	OW0	WAT	W	126	-6.804	14.466	42.289	1.00	27.19	8
ATOM	2215	OW0	WAT	W	127	24.517	14.294	40.806	1.00	27.26	8
ATOM	2216	OW0	WAT	W	128	-4.697	17.443	41.250	1.00	27.26	8
ATOM	2217	OW0	WAT	W	129	15.601	-5.581	15.252	1.00	27.49	8
ATOM	2218	OW0	WAT	W	130	19.225	-7.757	52.854	1.00	27.55	8
ATOM	2219	OW0	WAT	W	131	20.571	-7.244	23.187	1.00	27.79	8
ATOM	2220	OW0	WAT	W	132	-5.634	12.995	45.863	1.00	27.84	8
ATOM	2221	OW0	WAT	W	133	29.455	2.015	28.288	1.00	27.85	8
ATOM	2222	OW0	WAT	W	134	35.253	6.005	33.542	1.00	27.91	8
ATOM	2223	OW0	WAT	W	135	26.528	7.004	17.380	1.00	28.00	8
ATOM	2224	OW0	WAT	W	136	4.802	-2.134	53.088	1.00	28.06	8
ATOM	2225	OW0	WAT	W	137	7.702	-19.316	35.292	1.00	28.29	8
ATOM	2226	OW0	WAT	W	138	33.637	-3.892	43.427	1.00	28.32	8
ATOM	2227	OW0	WAT	W	139	-3.078	-11.204	41.616	1.00	28.34	8
ATOM	2228	OW0	WAT	W	140	7.296	-11.855	20.394	1.00	28.39	8
ATOM	2229	OW0	WAT	W	141	-8.355	14.458	38.156	1.00	28.47	8
ATOM	2230	OW0	WAT	W	142	-3.786	-10.077	45.809	1.00	28.51	8
ATOM	2231	OW0	WAT	W	143	17.884	8.271	55.001	1.00	28.52	8
ATOM	2232	OW0	WAT	W	144	-7.450	9.431	27.023	1.00	28.66	8
ATOM	2233	OW0	WAT	W	145	25.034	10.848	14.171	1.00	28.68	8

ATOM	2234	OW0	WAT	W	146	27.154	14.822	33.256	1.00	28.71	8
ATOM	2235	OW0	WAT	W	147	3.930	14.554	35.353	1.00	28.86	8
ATOM	2236	OW0	WAT	W	148	3.832	14.101	17.367	1.00	28.94	8
ATOM	2237	OW0	WAT	W	149	-7.141	6.522	26.433	1.00	28.95	8
ATOM	2238	OW0	WAT	W	150	16.291	15.441	37.748	1.00	28.96	8
ATOM	2239	OW0	WAT	W	151	23.732	-13.472	32.813	1.00	29.06	8
ATOM	2240	OW0	WAT	W	152	31.579	0.528	49.009	1.00	29.17	8
ATOM	2241	OW0	WAT	W	153	0.948	11.515	50.856	1.00	29.19	8
ATOM	2242	OW0	WAT	W	154	20.562	20.238	24.104	1.00	29.61	8
ATOM	2243	OW0	WAT	W	155	14.815	22.549	27.658	1.00	29.72	8
ATOM	2244	OW0	WAT	W	156	-0.505	13.461	15.844	1.00	29.79	8
ATOM	2245	OW0	WAT	W	157	27.503	-7.381	36.814	1.00	29.90	8
ATOM	2246	OW0	WAT	W	158	31.766	-7.236	46.577	1.00	29.96	8
ATOM	2247	OW0	WAT	W	159	2.280	5.918	54.243	1.00	30.06	8
ATOM	2248	OW0	WAT	W	160	15.109	18.191	36.248	1.00	30.13	8
ATOM	2249	OW0	WAT	W	161	4.637	-16.479	32.113	1.00	30.14	8
ATOM	2250	OW0	WAT	W	162	17.268	13.651	16.688	1.00	30.17	8
ATOM	2251	OW0	WAT	W	163	19.452	14.125	43.037	1.00	30.18	8
ATOM	2252	OW0	WAT	W	164	-4.171	13.696	26.886	1.00	30.24	8
ATOM	2253	OW0	WAT	W	165	14.909	-15.477	49.534	1.00	30.29	8
ATOM	2254	OW0	WAT	W	166	-8.602	11.318	30.557	1.00	30.42	8
ATOM	2255	OW0	WAT	W	167	19.207	-15.058	28.159	1.00	30.52	8
ATOM	2256	OW0	WAT	W	168	26.601	10.511	46.969	1.00	30.58	8
ATOM	2257	OW0	WAT	W	169	31.110	-8.170	41.359	1.00	30.61	8
ATOM	2258	OW0	WAT	W	170	29.593	8.135	46.349	1.00	30.72	8
ATOM	2259	OW0	WAT	W	171	-10.368	-1.876	34.504	1.00	30.74	8
ATOM	2260	OW0	WAT	W	172	28.564	-4.100	29.544	1.00	30.83	8
ATOM	2261	OW0	WAT	W	173	-12.777	4.044	45.410	1.00	30.92	8
ATOM	2262	OW0	WAT	W	174	7.794	-21.931	42.319	1.00	30.96	8
ATOM	2263	OW0	WAT	W	175	18.808	-10.251	23.688	1.00	31.07	8
ATOM	2264	OW0	WAT	W	176	0.113	-6.364	50.914	1.00	31.09	8
ATOM	2265	OW0	WAT	W	177	-3.585	3.671	16.785	1.00	31.12	8
ATOM	2266	OW0	WAT	W	178	4.754	-21.901	38.826	1.00	31.24	8
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ATOM	2269	OW0	WAT	W	181	19.204	-18.620	42.633	1.00	31.46	8
ATOM	2270	OW0	WAT	W	182	23.808	-11.495	40.059	1.00	31.53	8
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ATOM	2272	OW0	WAT	W	184	12.448	14.328	33.070	1.00	31.59	8
ATOM	2273	OW0	WAT	W	185	1.205	17.345	29.981	1.00	31.67	8
ATOM	2274	OW0	WAT	W	186	-9.791	7.997	34.844	1.00	31.75	8
ATOM	2275	OW0	WAT	W	187	-7.837	18.408	38.069	1.00	31.89	8
ATOM	2276	OW0	WAT	W	188	11.140	-9.008	50.792	1.00	31.95	8
ATOM	2277	OW0	WAT	W	189	26.511	-2.526	54.760	1.00	32.13	8
ATOM	2278	OW0	WAT	W	190	23.093	-7.348	24.192	1.00	32.27	8
ATOM	2279	OW0	WAT	W	191	-10.284	6.288	39.379	1.00	32.43	8
ATOM	2280	OW0	WAT	W	192	-7.821	-0.312	31.358	1.00	32.44	8
ATOM	2281	OW0	WAT	W	193	20.703	-19.058	40.128	1.00	32.50	8
ATOM	2282	OW0	WAT	W	194	23.085	18.180	25.298	1.00	32.52	8
ATOM	2283	OW0	WAT	W	195	18.564	11.924	14.883	1.00	32.61	8
ATOM	2284	OW0	WAT	W	196	19.725	-15.776	37.227	1.00	32.93	8
ATOM	2285	OW0	WAT	W	197	9.423	-12.850	50.029	1.00	33.07	8
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ATOM	2287	OW0	WAT	W	199	-10.872	11.311	41.622	1.00	33.34	8
ATOM	2288	OW0	WAT	W	200	24.953	-10.123	51.108	1.00	33.47	8
ATOM	2289	OW0	WAT	W	201	10.234	12.343	37.442	1.00	33.61	8
ATOM	2290	OW0	WAT	W	202	-1.385	9.325	49.590	1.00	33.68	8
ATOM	2291	OW0	WAT	W	203	13.133	-13.562	50.516	1.00	33.68	8
ATOM	2292	OW0	WAT	W	204	32.332	3.720	31.230	1.00	33.72	8
ATOM	2293	OW0	WAT	W	205	-4.769	19.603	30.890	1.00	34.01	8
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ATOM	2295	OW0	WAT	W	207	5.473	-14.541	47.418	1.00	34.18	8
ATOM	2296	OW0	WAT	W	208	-0.600	-4.653	18.959	1.00	34.35	8
ATOM	2297	OW0	WAT	W	209	5.122	13.867	48.979	1.00	34.37	8
ATOM	2298	OW0	WAT	W	210	-4.776	-9.796	38.696	1.00	34.40	8
ATOM	2299	OW0	WAT	W	211	22.711	8.507	56.151	1.00	34.54	8
ATOM	2300	OW0	WAT	W	212	-5.723	12.192	25.199	1.00	34.59	8
ATOM	2301	OW0	WAT	W	213	-5.854	7.368	47.036	1.00	34.60	8

```
ATOM   2302  OW0 WAT W 214       2.162  12.775  15.472  1.00 34.69    8
ATOM   2303  OW0 WAT W 215      29.086  -4.835  51.244  1.00 34.91    8
ATOM   2304  OW0 WAT W 216      29.521   1.500  30.290  1.00 35.03    8
ATOM   2305  OW0 WAT W 217       9.270  16.229  27.647  1.00 35.08    8
ATOM   2306  OW0 WAT W 218      -0.559 -13.990  44.942  1.00 35.09    8
ATOM   2307  OW0 WAT W 219      31.092  12.772  28.102  1.00 35.13    8
ATOM   2308  OW0 WAT W 220       4.053  17.330  40.649  1.00 35.18    8
ATOM   2309  OW0 WAT W 221       9.804  12.126  12.806  1.00 35.19    8
ATOM   2310  OW0 WAT W 222      16.382  10.037  14.084  1.00 35.33    8
ATOM   2311  OW0 WAT W 223      34.860   8.861  43.050  1.00 35.36    8
ATOM   2312  OW0 WAT W 224       2.481  -1.469  55.185  1.00 35.39    8
ATOM   2313  OW0 WAT W 225      27.639  15.901  20.220  1.00 35.45    8
ATOM   2314  OW0 WAT W 226      13.522  14.546  22.193  1.00 35.58    8
ATOM   2315  OW0 WAT W 227      18.759 -16.368  34.341  1.00 35.64    8
ATOM   2316  OW0 WAT W 228      29.746   6.054  47.983  1.00 35.88    8
ATOM   2317  OW0 WAT W 229       1.824   8.703  50.441  1.00 35.91    8
ATOM   2318  OW0 WAT W 230       4.304 -10.212  20.566  1.00 36.11    8
ATOM   2319  OW0 WAT W 231      25.903  -4.307  53.039  1.00 36.25    8
ATOM   2320  OW0 WAT W 232      30.041  -9.858  50.314  1.00 36.32    8
ATOM   2321  OW0 WAT W 233       2.098   9.375  12.724  1.00 36.32    8
ATOM   2322  OW0 WAT W 234      -6.517 -10.587  46.846  1.00 36.56    8
ATOM   2323  OW0 WAT W 235      -6.610  -3.836  30.415  1.00 36.57    8
ATOM   2324  OW0 WAT W 236     -10.495  12.363  34.899  1.00 36.64    8
ATOM   2325  OW0 WAT W 237      -9.368   9.062  33.012  1.00 36.76    8
ATOM   2326  OW0 WAT W 238      19.878  23.075  33.288  1.00 36.92    8
ATOM   2327  OW0 WAT W 239      -4.530   7.046  20.896  1.00 36.93    8
ATOM   2328  OW0 WAT W 240      33.313   6.152  46.202  1.00 36.93    8
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ATOM   2330  OW0 WAT W 242      -0.158  -8.511  20.728  1.00 37.69    8
ATOM   2331  OW0 WAT W 243       5.833  13.274  13.596  1.00 37.75    8
ATOM   2332  OW0 WAT W 244       5.857 -19.503  31.198  1.00 37.77    8
ATOM   2333  OW0 WAT W 245      -2.468 -11.125  30.496  1.00 37.88    8
ATOM   2334  OW0 WAT W 246       8.010 -18.250  25.554  1.00 37.97    8
ATOM   2335  OW0 WAT W 247      -2.981  10.860  22.607  1.00 38.01    8
ATOM   2336  OW0 WAT W 248      29.733   2.478  51.185  1.00 38.06    8
ATOM   2337  OW0 WAT W 249      -1.876  18.713  35.692  1.00 38.18    8
ATOM   2338  OW0 WAT W 250      -0.040  -2.395  54.365  1.00 38.20    8
ATOM   2339  OW0 WAT W 251      -2.499  -1.254  18.143  1.00 38.26    8
ATOM   2340  OW0 WAT W 252       1.301  15.936  18.064  1.00 38.65    8
ATOM   2341  OW0 WAT W 253      -7.703   5.024  28.841  1.00 38.66    8
ATOM   2342  OW0 WAT W 254       8.197 -10.548  51.105  1.00 38.97    8
ATOM   2343  OW0 WAT W 255      19.072  -5.777  16.600  1.00 39.02    8
ATOM   2344  OW0 WAT W 256      -1.755  -6.479  25.704  1.00 39.11    8
ATOM   2345  OW0 WAT W 257      15.948 -20.846  38.342  1.00 39.37    8
ATOM   2346  OW0 WAT W 258      -7.884  13.866  29.148  1.00 39.59    8
ATOM   2347  OW0 WAT W 259      34.511  11.821  32.723  1.00 39.65    8
ATOM   2348  OW0 WAT W 260      16.479 -16.084  27.952  1.00 39.69    8
ATOM   2349  OW0 WAT W 261      -8.601   2.060  30.456  1.00 39.87    8
ATOM   2350  OW0 WAT W 262      -0.861  17.301  21.849  1.00 39.89    8
ATOM   2351  OW0 WAT W 263       8.555 -18.275  47.241  1.00 39.93    8
ATOM   2352  OW0 WAT W 264      24.230  -5.252  22.664  1.00 40.00    8
ATOM   2353  OW0 WAT W 265      -1.056   0.937  53.921  1.00 40.53    8
ATOM   2354  OW0 WAT W 266      16.017 -13.902  22.326  1.00 40.63    8
ATOM   2355  OW0 WAT W 267      23.066  10.127  50.334  1.00 40.86    8
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ATOM   2361  OW0 WAT W 273       6.542  -6.740  51.852  1.00 42.53    8
ATOM   2362  OW0 WAT W 274      13.730  15.335  37.537  1.00 42.69    8
ATOM   2363  OW0 WAT W 275      25.430   5.894  14.816  1.00 42.71    8
ATOM   2364  OW0 WAT W 276      -6.269   3.726  22.288  1.00 43.87    8
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ATOM   2367  OW0 WAT W 279      22.549  19.383  22.028  1.00 44.26    8
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ATOM   2369  OW0 WAT W 281      12.425  -9.624  21.392  1.00 45.09    8
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ATOM   2370  OW0 WAT W 282       9.040  -7.996  13.289  1.00 45.24    8
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ATOM   2375  OW0 WAT W 287      16.268  22.912  35.142  1.00 47.83    8
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ATOM   2377  OW0 WAT W 289      30.772  12.835  22.683  1.00 49.34    8
ATOM   2378  OW0 WAT W 290      22.334  12.132  49.136  1.00 49.76    8
ATOM   2379  OW0 WAT W 291      -9.173  -1.103  47.956  1.00 50.16    8
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Patent Claims

1. A polypeptide with reduced immune response, having one or more amino acid residues modified, wherein the C^{α}-atoms of said amino acid residues are located less than 15 Å from a ligand bound to said polypeptide.

2. A polypeptide according to claim 1, wherein the polypeptide has reduced allergenicity.

3. The polypeptide according to any of the claims 1 to 2, wherein the C^{β}-atom of the amino acid residues is located closer to the ligand than the C^{α}-atom.

4. The polypeptide according to any of the claims 1 to 3, wherein the C^{α}-atoms of the amino acid residues are located less than 10 Å from the ligand and said amino acid residues have an accessibility of at least 15%.

5. The polypeptide according to any of the claims 1 to 4, wherein the ligand is a metal or metal ion.

6. The polypeptide according to any of the preceding claims, wherein the polypeptide is modified by substitution of amino acid residues.

7. The polypeptide according to any of the claims 1 to 6, wherein the modified polypeptide has been selected from a diverse library of variants.

8. The polypeptide according to claim 6, wherein the substituting amino acids contain amino groups in the form of Lysine residues(s), or carboxylic groups in the form of Aspartic acid or Glutamic acid residues, or SH-groups in the form of Cysteine residues.

9. The polypeptide according to claim 6, wherein the modification(s) is(are) prepared by a conservative substitution of an amino acid residue, such as an Arginine to Lysine substitution or Aspargine to Aspartate/Glutamate or a Glutamine to Aspartate/Glutamate substitution or Threonine/Serine to Cysteine.

10. The polypeptide according to claims 1-9, wherein the polypeptide is modified by coupling one or more polymeric molecules to said polypeptide, thereby providing a polypeptide-

polymer conjugate.

11. The polypeptide according to claim 10, wherein the parent polypeptide moiety of the conjugate has a molecular weight from 1 to 1000 kDa, preferred 4 to 100 kDa, more preferred 12 to 60 kDa.

12. The polypeptide according to claim 10, wherein the polymeric molecules coupled to the polypeptide have a molecular weight from 0.1 to 100, preferably 0.1 to 60 kDa, more preferably 0.3-5 kDa, most preferably 1 to 2 kDa.

13. The polypeptide according to any of the preceding claims, wherein said polypeptide or parent polypeptide is an enzyme selected from the group of Oxidoreductases, including laccases and Superoxide dismutase (SOD); Hydrolases, including carbohydrases, amylases, proteases, especially subtilisins; Transferases, including Transglutaminases (TGases); Isomerases, including Protein disulfide Isomerases (PDI); Lyases, including Pectate lyases.

14. The polypeptide according to claim 13, wherein said polypeptide or parent polypeptide is PD498, Savinase®, BPN´, Amylase, Proteinase K, Proteinase R, Subtilisin DY, Lion Y, Rennilase®, JA16, Alcalase®.

15. The polypeptide according to claim 14, wherein the polypeptide or parent polypeptide of the conjugate is a PD498 variant with one or more of the following substitutions: The amino acid residues in position 86, 87, 7, 47, 51, 219, 12, 218, 10, 11, 53, 28, 1, 65, 61, 63, 67, 60, 69, 55, 44, 45, 111, 115, 109, 215, 200, 202, 170, 268, 250, 152, 254, 136, 269, 246, 141 is substituted with K, D, E, or C, preferably R250K, R250D, R250E, R250C.

16. The polypeptide according to claim 14, wherein the polypeptide or parent polypeptide is a BPN´ variant with one or more of the following substitutions: The amino acid residues in position 77, 2, 5, 43, 214, 206, 22, 215, 14, 17, 9, 36, 211, 195, 197, 154, 163, 247, 265, 251, 143, 127, 260, 131, 128, 243 is substituted with K, D, E, or C, preferably R247K, R247D, R247E, R247C.

17. The polypeptide according to claim 14, wherein the polypeptide or parent polypeptide is a Savinase® variant with

one or more of the following substitutions: The amino acid residues in position 75, 2, 42, 208, 200, 14, 22, 17, 189, 241, 125, 125, 141, 245, 259, 237, 254, 157 is substituted with K, D, E, or C, preferably R241K, R241D, R241E, R241C.

18. The polypeptide according to claim 14, wherein the polypeptide or parent polypeptide is an amylase variant with one or more of the following substitutions: The amino acid residue in position 124, 126, 128, 159, 160, 166, 185, 186, 189, 190, 193, 194, 195, 196, 198, 201, 202, 203, 209, 210, 214, 242, 244, 247, 296, 298, 299, 302, 303, 304, 306, 307, 308, 310, 311, 314, 345, 347, 405, 406, 407, 408, 409, 433, 434, 435, 436, 437, 475, 476, 477, 478 is substituted with K, D, E, or C.

19. The polypeptide according to claims 10 or 12, wherein the polymeric molecule is selected from the group comprising a natural or synthetic homo- and heteropolymers, selected from the group of the synthetic polymeric molecules including Branched PEGs, poly-vinyl alcohol (PVA), poly-carboxyl acids, poly-(vinylpyrolidone) and poly-D,L-amino acids, or natural occurring polymeric molecules including dextrans, including carboxymethyl-dextrans, and celluloses such as methylcellulose, carboxymethylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, and hydrolysates of chitosan, starches, such as hydroxyethyl-starches, hydroxypropyl-starches, glycogen, agarose, guar gum, inulin, pullulans, xanthan gums, carrageenin, pectin and alginic acid.

20. The polypeptide according to claim 19, wherein the modified polypeptide is savinase variant R241KbPEG1000 or R241KbPEG2000.

21. The polypeptide according to any of claims 1 to 7, wherein the modified polypeptide is savinase variants R241Q, R241E, R241H or R241K.

22. A method for preparing polypeptides with reduced immune response comprising the steps of:

a) identifying amino acid residues located on the surface of the 3-dimensional structure of the parent polypeptide in question,

b) selecting target amino acid residues on the surface of said 3-dimensional structure of said parent polypeptide to be modified,

c) substituting one or more amino acid residues selected in step b) with other amino acid residues, and/or

d) coupling polymeric molecules to the amino acid residues in step b) and/or step c).

23. The method according to claim 22, wherein the C^{α}-atoms of the amino acid residues are located less than 15 Å from the ligand bound to said polypeptide.

24. The method according to any of claims 22 to 23, wherein the C^{β}-atoms of the amino acid residues are located closer to the ligand than the C^{α}-atom.

25. The method according to any of the claims 22-24, wherein the C^{α}-atoms of the amino acid residues are located less than 10 Å from the ligand and said amino acid residues have an accessibility of at least 15%, preferable at least 20%, more preferably at least 30%.

26. The method according to any of the claims 22-25, wherein the identification of amino acid residues located on the surface on the polypeptide referred to in step a) are performed by a computer program analyzing the 3-dimensional structure of the parent polypeptide in question.

27. The method according to any of the claims 22 to 26, wherein step b) comprises selecting Arginine or Lysine residues on the surface of the parent polypeptide.

28. The method according to claim 27, wherein one or more Arginine residues identified in step b) is(are) substituted with a Lysine residue(s) in step c).

29. Use of the modified polypeptide in claims 1 to 21 for reducing the allergenicity of industrial products.

30. Use of the modified polypeptide in claims 1 to 21 for reducing the immunogenicity of pharmaceuticals.

31. A composition comprising a modified polypeptide of any of claims 1 to 21 and further comprising ingredients used in industrial products.

32. The composition according to claim 31, wherein the industrial product is a detergent, such as a laundry, dish wash or hard surface cleaning product, including bio-film products or a food or feed product or a textile product.

33. The composition according to claim 32, comprising a modified polypeptide of any of claims 1 to 21 and further ingredients used in personal care products, especially skin care products.

34. A composition comprising a modified polypeptide of any of claims 1 to 21 and further comprising ingredients used in pharmaceuticals.

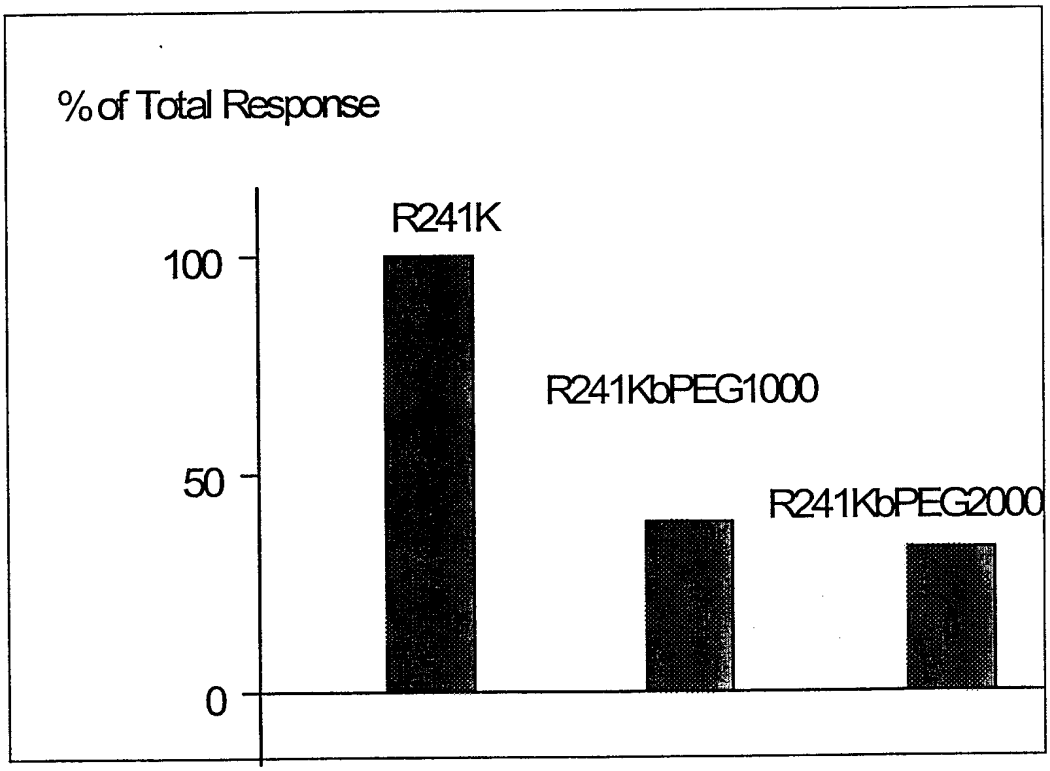
% of Total Response
100
50
0
R241K
R241KbPEG1000
R241KbPEG2000

Fig. 1

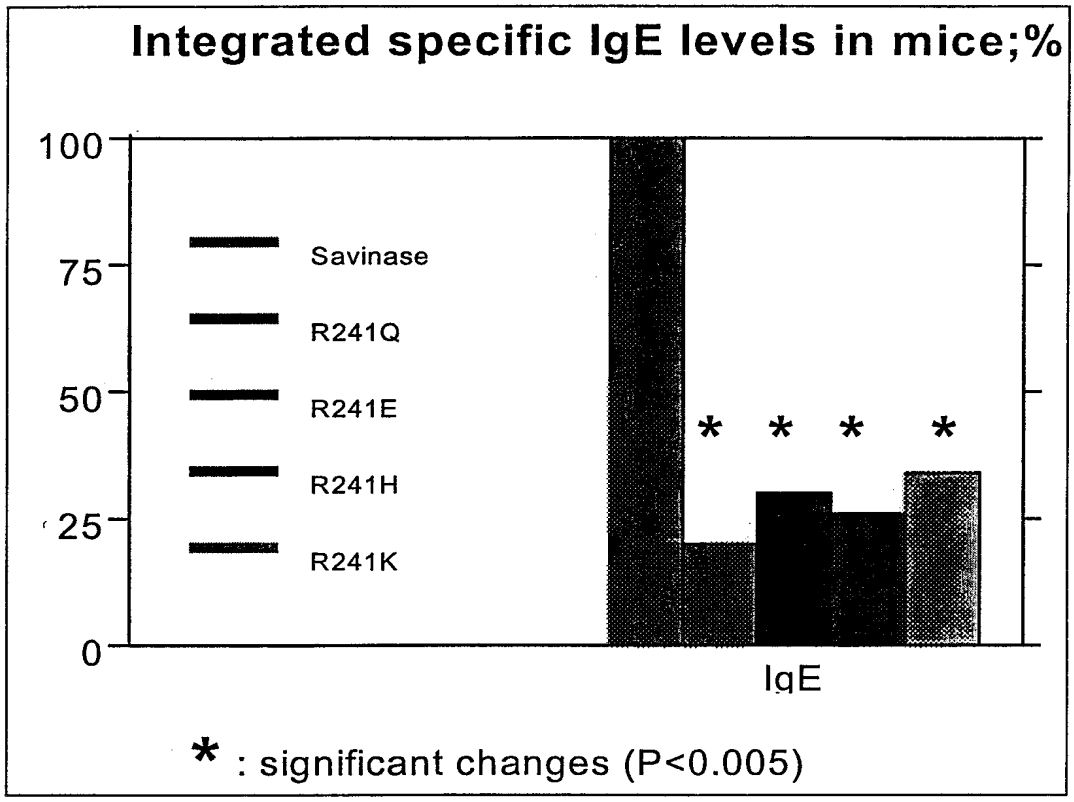
Integrated specific IgE levels in mice;%
100
75
50
25
0
Savinase
R241Q
R241E
R241H
R241K
* * * *
IgE
* : significant changes (P<0.005)

Fig. 2

SEQUENCE LISTING

(1) GENERAL INFORMATION:
(i) APPLICANT:
(A) NAME: Novo Nordisk A/S
(B) STREET: Novo Alle
(C) CITY: Bagsveard
(E) COUNTRY: Denmark
(F) POSTAL CODE (ZIP): DK-2880
(G) TELEPHONE: +45 4444 8888
(H) TELEFAX: +45 4449 3256
(ii) TITLE OF INVENTION: A modified polypeptide
(iii) NUMBER OF SEQUENCES: 9
(iv) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)

(2) INFORMATION FOR SEQ ID NO: 1:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 840 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(vi) ORIGINAL SOURCE:
(B) STRAIN: Bacillus sp. PD498, NCIMB No. 40484
(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION:1..840
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

```
TGG TCA CCG AAT GAC CCT TAC TAT TCT GCT TAC CAG TAT GGA CCA CAA        48
Trp Ser Pro Asn Asp Pro Tyr Tyr Ser Ala Tyr Gln Tyr Gly Pro Gln
  1               5                  10                  15

AAC ACC TCA ACC CCT GCT GCC TGG GAT GTA ACC CGT GGA AGC AGC ACT        96
Asn Thr Ser Thr Pro Ala Ala Trp Asp Val Thr Arg Gly Ser Ser Thr
             20                  25                  30

CAA ACG GTG GCG GTC CTT GAT TCC GGA GTG GAT TAT AAC CAC CCT GAT       144
Gln Thr Val Ala Val Leu Asp Ser Gly Val Asp Tyr Asn His Pro Asp
         35                  40                  45

CTT GCA AGA AAA GTA ATA AAA GGG TAC GAC TTT ATC GAC AGG GAC AAT       192
Leu Ala Arg Lys Val Ile Lys Gly Tyr Asp Phe Ile Asp Arg Asp Asn
     50                  55                  60

AAC CCA ATG GAT CTT AAC GGA CAT GGT ACC CAT GTT GCC GGT ACT GTT       240
Asn Pro Met Asp Leu Asn Gly His Gly Thr His Val Ala Gly Thr Val
 65                  70                  75                  80

GCT GCT GAT ACG AAC AAT GGA ATT GGC GTA GCC GGT ATG GCA CCA GAT       288
Ala Ala Asp Thr Asn Asn Gly Ile Gly Val Ala Gly Met Ala Pro Asp
                 85                  90                  95

ACG AAG ATC CTT GCC GTA CGG GTC CTT GAT GCC AAT GGA AGT GGC TCA       336
Thr Lys Ile Leu Ala Val Arg Val Leu Asp Ala Asn Gly Ser Gly Ser
            100                 105                 110
```

```
CTT GAC AGC ATT GCC TCA GGT ATC CGC TAT GCT GCT GAT CAA GGG GCA        384
Leu Asp Ser Ile Ala Ser Gly Ile Arg Tyr Ala Ala Asp Gln Gly Ala
        115                 120                 125

AAG GTA CTC AAC CTC TCC CTT GGT TGC GAA TGC AAC TCC ACA ACT CTT        432
Lys Val Leu Asn Leu Ser Leu Gly Cys Glu Cys Asn Ser Thr Thr Leu
    130                 135                 140

AAG AGT GCC GTC GAC TAT GCA TGG AAC AAA GGA GCT GTA GTC GTT GCT        480
Lys Ser Ala Val Asp Tyr Ala Trp Asn Lys Gly Ala Val Val Val Ala
145                 150                 155                 160

GCT GCA GGG AAT GAC AAT GTA TCC CGT ACA TTC CAA CCA GCT TCT TAC        528
Ala Ala Gly Asn Asp Asn Val Ser Arg Thr Phe Gln Pro Ala Ser Tyr
                165                 170                 175

CCT AAT GCC ATT GCA GTA GGT GCC ATT GAC TCC AAT GAT CGA AAA GCA        576
Pro Asn Ala Ile Ala Val Gly Ala Ile Asp Ser Asn Asp Arg Lys Ala
            180                 185                 190

TCA TTC TCC AAT TAC GGA ACG TGG GTG GAT GTC ACT GCT CCA GGT GTG        624
Ser Phe Ser Asn Tyr Gly Thr Trp Val Asp Val Thr Ala Pro Gly Val
        195                 200                 205

AAC ATA GCA TCA ACC GTT CCG AAT AAT GGC TAC TCC TAC ATG TCT GGT        672
Asn Ile Ala Ser Thr Val Pro Asn Asn Gly Tyr Ser Tyr Met Ser Gly
    210                 215                 220

ACG TCC ATG GCA TCC CCT CAC GTG GCC GGT TTG GCT GCT TTG TTG GCA        720
Thr Ser Met Ala Ser Pro His Val Ala Gly Leu Ala Ala Leu Leu Ala
225                 230                 235                 240

AGT CAA GGT AAG AAT AAC GTA CAA ATC CGC CAG GCC ATT GAG CAA ACC        768
Ser Gln Gly Lys Asn Asn Val Gln Ile Arg Gln Ala Ile Glu Gln Thr
                245                 250                 255

GCC GAT AAG ATC TCT GGC ACT GGA ACA AAC TTC AAG TAT GGT AAA ATC        816
Ala Asp Lys Ile Ser Gly Thr Gly Thr Asn Phe Lys Tyr Gly Lys Ile
            260                 265                 270

AAC TCA AAC AAA GCT GTA AGA TAC                                       840
Asn Ser Asn Lys Ala Val Arg Tyr
        275                 280
```

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 280 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

```
Trp Ser Pro Asn Asp Pro Tyr Tyr Ser Ala Tyr Gln Tyr Gly Pro Gln
  1               5                  10                  15

Asn Thr Ser Thr Pro Ala Ala Trp Asp Val Thr Arg Gly Ser Ser Thr
             20                  25                  30
```

```
Gln Thr Val Ala Val Leu Asp Ser Gly Val Asp Tyr Asn His Pro Asp
         35                  40                  45

Leu Ala Arg Lys Val Ile Lys Gly Tyr Asp Phe Ile Asp Arg Asp Asn
     50                  55                  60

Asn Pro Met Asp Leu Asn Gly His Gly Thr His Val Ala Gly Thr Val
 65                  70                  75                  80

Ala Ala Asp Thr Asn Asn Gly Ile Gly Val Ala Gly Met Ala Pro Asp
                 85                  90                  95

Thr Lys Ile Leu Ala Val Arg Val Leu Asp Ala Asn Gly Ser Gly Ser
            100                 105                 110

Leu Asp Ser Ile Ala Ser Gly Ile Arg Tyr Ala Ala Asp Gln Gly Ala
        115                 120                 125

Lys Val Leu Asn Leu Ser Leu Gly Cys Glu Cys Asn Ser Thr Thr Leu
    130                 135                 140

Lys Ser Ala Val Asp Tyr Ala Trp Asn Lys Gly Ala Val Val Val Ala
145                 150                 155                 160

Ala Ala Gly Asn Asp Asn Val Ser Arg Thr Phe Gln Pro Ala Ser Tyr
                165                 170                 175

Pro Asn Ala Ile Ala Val Gly Ala Ile Asp Ser Asn Asp Arg Lys Ala
            180                 185                 190

Ser Phe Ser Asn Tyr Gly Thr Trp Val Asp Val Thr Ala Pro Gly Val
        195                 200                 205

Asn Ile Ala Ser Thr Val Pro Asn Asn Gly Tyr Ser Tyr Met Ser Gly
    210                 215                 220

Thr Ser Met Ala Ser Pro His Val Ala Gly Leu Ala Ala Leu Leu Ala
225                 230                 235                 240

Ser Gln Gly Lys Asn Asn Val Gln Ile Arg Gln Ala Ile Glu Gln Thr
                245                 250                 255

Ala Asp Lys Ile Ser Gly Thr Gly Thr Asn Phe Lys Tyr Gly Lys Ile
            260                 265                 270

Asn Ser Asn Lys Ala Val Arg Tyr
        275                 280
```

(2) INFORMATION FOR SEQ ID NO: 3:
  (i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 269 amino acids
    (B) TYPE: amino acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear
  (ii) MOLECULE TYPE: protein
  (vi) ORIGINAL SOURCE:
    (B) STRAIN: Bacillus lentus
  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

```
Ala Gln Ser Val Pro Trp Gly Ile Ser Arg Val Gln Ala Pro Ala Ala
```

```
1               5                   10                  15

His Asn Arg Gly Leu Thr Gly Ser Gly Val Lys Val Ala Val Leu Asp
            20                  25                  30

Thr Gly Ile Ser Thr His Pro Asp Leu Asn Ile Arg Gly Gly Ala Ser
        35                  40                  45

Phe Val Pro Gly Glu Pro Ser Thr Gln Asp Gly Asn Gly His Gly Thr
    50                  55                  60

His Val Ala Gly Thr Ile Ala Ala Leu Asn Asn Ser Ile Gly Val Leu
65                  70                  75                  80

Gly Val Ala Pro Ser Ala Glu Leu Tyr Ala Val Lys Val Leu Gly Ala
                85                  90                  95

Ser Gly Ser Gly Ser Val Ser Ser Ile Ala Gln Gly Leu Glu Trp Ala
            100                 105                 110

Gly Asn Asn Gly Met His Val Ala Asn Leu Ser Leu Gly Ser Pro Ser
        115                 120                 125

Pro Ser Ala Thr Leu Glu Gln Ala Val Asn Ser Ala Thr Ser Arg Gly
    130                 135                 140

Val Leu Val Val Ala Ala Ser Gly Asn Ser Gly Ala Gly Ser Ile Ser
145                 150                 155                 160

Tyr Pro Ala Arg Tyr Ala Asn Ala Met Ala Val Gly Ala Thr Asp Gln
                165                 170                 175

Asn Asn Asn Arg Ala Ser Phe Ser Gln Tyr Gly Ala Gly Leu Asp Ile
            180                 185                 190

Val Ala Pro Gly Val Asn Val Gln Ser Thr Tyr Pro Gly Ser Thr Tyr
        195                 200                 205

Ala Ser Leu Asn Gly Thr Ser Met Ala Thr Pro His Val Ala Gly Ala
    210                 215                 220

Ala Ala Leu Val Lys Gln Lys Asn Pro Ser Trp Ser Asn Val Gln Ile
225                 230                 235                 240

Arg Asn His Leu Lys Asn Thr Ala Thr Ser Leu Gly Ser Thr Asn Leu
                245                 250                 255

Tyr Gly Ser Gly Leu Val Asn Ala Glu Ala Ala Thr Arg
            260                 265
```

(2) INFORMATION FOR SEQ ID NO: 4:
  (i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 1458 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear
  (ii) MOLECULE TYPE: DNA (genomic)
  (vi) ORIGINAL SOURCE:

(B) STRAIN: Bacillus sp. DSM No. 12649
(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION:1..1458
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

```
cac cat aat ggt acg aac ggc aca atg atg cag tac ttt gaa tgg tat      48
 His His Asn Gly Thr Asn Gly Thr Met Met Gln Tyr Phe Glu Trp Tyr
  1               5                  10                  15

cta cca aat gac gga aac cat tgg aat aga tta agg tct gat gca agt      96
 Leu Pro Asn Asp Gly Asn His Trp Asn Arg Leu Arg Ser Asp Ala Ser
              20                  25                  30

aac cta aaa gat aaa ggg atc tca gcg gtt tgg att cct cct gca tgg     144
 Asn Leu Lys Asp Lys Gly Ile Ser Ala Val Trp Ile Pro Pro Ala Trp
          35                  40                  45

aag ggt gcc tct caa aat gat gtg ggg tat ggt gct tat gat ctg tat     192
 Lys Gly Ala Ser Gln Asn Asp Val Gly Tyr Gly Ala Tyr Asp Leu Tyr
      50                  55                  60

gat tta gga gaa ttc aat caa aaa gga acc att cgt aca aaa tat gga     240
 Asp Leu Gly Glu Phe Asn Gln Lys Gly Thr Ile Arg Thr Lys Tyr Gly
  65                  70                  75                  80

acg cgc aat cag tta caa gct gca gtt aac gcc ttg aaa agt aat gga     288
 Thr Arg Asn Gln Leu Gln Ala Ala Val Asn Ala Leu Lys Ser Asn Gly
                  85                  90                  95

att caa gtg tat ggc gat gtt gta atg aat cat aaa ggg gga gca gac     336
 Ile Gln Val Tyr Gly Asp Val Val Met Asn His Lys Gly Gly Ala Asp
              100                 105                 110

gct acc gaa atg gtt agg gca gtt gaa gta aac ccg aat aat aga aat     384
 Ala Thr Glu Met Val Arg Ala Val Glu Val Asn Pro Asn Asn Arg Asn
          115                 120                 125

caa gaa gtg tcc ggt gaa tat aca att gag gct tgg aca aag ttt gac     432
 Gln Glu Val Ser Gly Glu Tyr Thr Ile Glu Ala Trp Thr Lys Phe Asp
      130                 135                 140
```

```
ttt cca gga cga ggt aat act cat tca aac ttc aaa tgg aga tgg tat      480
Phe Pro Gly Arg Gly Asn Thr His Ser Asn Phe Lys Trp Arg Trp Tyr
145                 150                 155                 160

cac ttt gat gga gta gat tgg gat cag tca cgt aag ctg aac aat cga      528
His Phe Asp Gly Val Asp Trp Asp Gln Ser Arg Lys Leu Asn Asn Arg
                165                 170                 175

att tat aaa ttt aga ggt gat gga aaa ggg tgg gat tgg gaa gtc gat      576
Ile Tyr Lys Phe Arg Gly Asp Gly Lys Gly Trp Asp Trp Glu Val Asp
            180                 185                 190

aca gaa aac ggt aac tat gat tac cta atg tat gca gat att gac atg      624
Thr Glu Asn Gly Asn Tyr Asp Tyr Leu Met Tyr Ala Asp Ile Asp Met
        195                 200                 205

gat cac cca gag gta gtg aat gag cta aga aat tgg ggt gtt tgg tat      672
Asp His Pro Glu Val Val Asn Glu Leu Arg Asn Trp Gly Val Trp Tyr
    210                 215                 220

acg aat aca tta ggc ctt gat ggt ttt aga ata gat gca gta aaa cat      720
Thr Asn Thr Leu Gly Leu Asp Gly Phe Arg Ile Asp Ala Val Lys His
225                 230                 235                 240

ata aaa tac agc ttt act cgt gat tgg att aat cat gtt aga agt gca      768
Ile Lys Tyr Ser Phe Thr Arg Asp Trp Ile Asn His Val Arg Ser Ala
                245                 250                 255

act ggc aaa aat atg ttt gcg gtt gcg gaa ttt tgg aaa aat gat tta      816
Thr Gly Lys Asn Met Phe Ala Val Ala Glu Phe Trp Lys Asn Asp Leu
            260                 265                 270

ggt gct att gaa aac tat tta aac aaa aca aac tgg aac cat tca gtc      864
Gly Ala Ile Glu Asn Tyr Leu Asn Lys Thr Asn Trp Asn His Ser Val
        275                 280                 285

ttt gat gtt ccg ctg cac tat aac ctc tat aat gct tca aaa agc gga      912
Phe Asp Val Pro Leu His Tyr Asn Leu Tyr Asn Ala Ser Lys Ser Gly
    290                 295                 300
```

```
ggg aat tat gat atg agg caa ata ttt aat ggt aca gtc gtg caa aga      960
Gly Asn Tyr Asp Met Arg Gln Ile Phe Asn Gly Thr Val Val Gln Arg
305                 310                 315                 320

cat cca atg cat gct gtt aca ttt gtt gat aat cat gat tcg caa cct     1008
His Pro Met His Ala Val Thr Phe Val Asp Asn His Asp Ser Gln Pro
                325                 330                 335

gaa gaa gct tta gag tct ttt gtt gaa gaa tgg ttc aaa cca tta gcg     1056
Glu Glu Ala Leu Glu Ser Phe Val Glu Glu Trp Phe Lys Pro Leu Ala
            340                 345                 350

tat gct ttg aca tta aca cgt gaa caa ggc tac cct tct gta ttt tat     1104
Tyr Ala Leu Thr Leu Thr Arg Glu Gln Gly Tyr Pro Ser Val Phe Tyr
        355                 360                 365

gga gat tat tat ggc att cca acg cat ggt gta cca gcg atg aaa tcg     1152
Gly Asp Tyr Tyr Gly Ile Pro Thr His Gly Val Pro Ala Met Lys Ser
    370                 375                 380

aaa att gac ccg att cta gaa gcg cgt caa aag tat gca tat gga aga     1200
Lys Ile Asp Pro Ile Leu Glu Ala Arg Gln Lys Tyr Ala Tyr Gly Arg
385                 390                 395                 400

caa aat gac tac tta gac cat cat aat atc atc ggt tgg aca cgt gaa     1248
Gln Asn Asp Tyr Leu Asp His His Asn Ile Ile Gly Trp Thr Arg Glu
                405                 410                 415

ggg aat aca gca cac ccc aac tcc ggt tta gct act atc atg tcc gat     1296
Gly Asn Thr Ala His Pro Asn Ser Gly Leu Ala Thr Ile Met Ser Asp
            420                 425                 430

ggg gca gga gga aat aag tgg atg ttt gtt ggg cgt aat aaa gct ggt     1344
Gly Ala Gly Gly Asn Lys Trp Met Phe Val Gly Arg Asn Lys Ala Gly
        435                 440                 445

caa gtt tgg acc gat atc act gga aat cgt gca ggt act gtt acg att     1392
Gln Val Trp Thr Asp Ile Thr Gly Asn Arg Ala Gly Thr Val Thr Ile
    450                 455                 460
```

```
aat gct gat gga tgg ggt aat ttt tct gta aat gga gga tca gtt tct     1440
Asn Ala Asp Gly Trp Gly Asn Phe Ser Val Asn Gly Gly Ser Val Ser
465                 470                 475                 480

att tgg gta aac aaa taa                                         1458
Ile Trp Val Asn Lys  *
                485
```

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 99/00542

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: C12N 9/96 // C11D 3/386, A61K 47/48
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 9835026 A1 (NOVO NORDISK A/S), 13 August 1998 (13.08.98), page 5; page 22, line 15 - line 17; page 24	1-34
	--	
X	WO 9830682 A1 (NOVO NORDISK A/S), 16 July 1998 (16.07.98), claims 1-2	1-34
	--	
A	WO 9730148 A1 (NOVO NORDISK A/S), 21 August 1997 (21.08.97)	1-34
	--	
A	WO 9617929 A1 (NOVO NORDISK A/S), 13 June 1996 (13.06.96)	1-34
	--	

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" erlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
31 January 2000	07 -02- 2000
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Yvonne Siösteen/EÖ Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 99/00542

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 9640792 A1 (NOVO NORDISK A/S), 19 December 1996 (19.12.96) --	1-34
A	Proc. Natl. Acad. Sci., Volume 88, August 1991, Michael S. Hershfield et al, "Use of site-directed mutagenesis to enhance the epitope-shielding effect of covalent modification of proteins with polyethylene glycol" page 7185 - page 7189 -- --------	1-34

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/DK 99/00542

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9835026 A1	13/08/98	AU 5749598 A	26/08/98
WO 9830682 A1	16/07/98	AU 5478598 A	03/08/98
		EP 0954572 A	10/11/99
WO 9730148 A1	21/08/97	AU 1540697 A	02/09/97
		CA 2242488 A	21/08/97
		CN 1211278 A	17/03/99
		EP 0894128 A	03/02/99
WO 9617929 A1	13/06/96	AU 697440 B	08/10/98
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		BR 9509976 A	09/06/98
		CA 2206852 A	13/06/96
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		EP 0796324 A	24/09/97
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		US 5856451 A	05/01/99
		US 5981718 A	09/11/99
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